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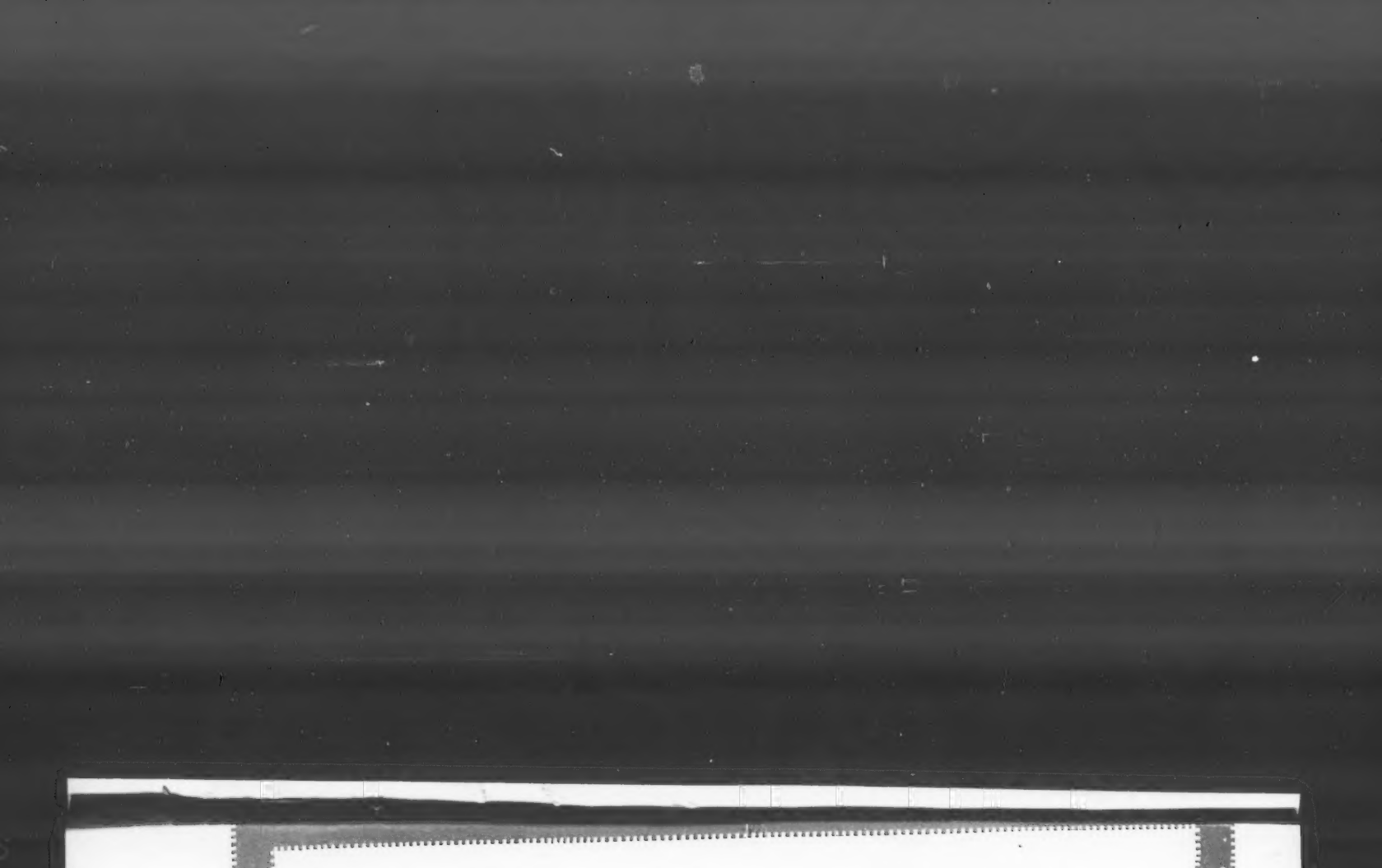

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THE

AMERICAN JOURNAL

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JANUARY, 1916.

ORIGINAL ARTICLES

OPEN-AIR TREATMENT OF PNUEMONIA AND ANEMIA IN CHILDREN.[1]

By Rowland G. Freeman, M.D.,

NEW YORK.

The importance of fresh air in the treatment of certain diseases is now well established. The best results from fresh-air treatment are obtained when the air is cold, when it is freely moving in an open space, and when the individual is kept in it twenty-four hours a day.

Little children tolerate poorly the stagnant air of most American houses in winter, and while inappropriate food is perhaps the most important cause of sickness in children, housing in winter is a close second. Severe cases of rachitis develop only in winter and in climates where babies are kept housed, and they develop under these conditions no matter what the food: and children of an ancestry from tropical climates suffer more from the housing than others, notably negroes and Italians.

Between the close, stagnant, indoor air that induces rachitis and pneumonia and the free-flowing, outdoor air there are many gradations due to methods of ventilation. The scientific forced ventilation which is interfered with by the opening of windows is expensive, occupies much space, and is usually inefficient. Open windows give a freshness to the air of a room that is never attained by scientific forced ventilation. The fear of a draught has been

[1] Read before the Association of American Physicians, Washington, D. C., May 12, 1915.

deeply impressed on all the last generation and many of the present. Too much access of air for comfort is best avoided by cheese-cloth screens. These were used many years ago by Henry Hun in the Albany Children's Hospital, and are today more satisfactory, I believe, than the patent ventilators made to place under an elevated window sash. In Dr. Hun's Hospital each window had two sets of sash, one pair carrying glass and the other cheese-cloth. The windows were usually kept open, the air entering freely through the cheese-cloth sash. These wards were always fresh and free from hospital odors, and the children in this institution did wonderfully well. While this method gives one perhaps the best indoor air for those requiring warm, still air, one may obtain far better results in the cold, fresh, outdoor air in winter.

It has long been an accepted fact among certain specialists in diseases of children that exposure to fresh, cold, moving air stimulates the circulation, puts color in the cheeks, increases the vigor of the body, the appetite, and the assimilation of food. While this has been applied particularly to children sick with a limited range of illness, especially pneumonia and tuberculosis, equally good results are derived from the use of this outdoor fresh-air treatment in bronchitis, anemia, chorea, marasmus, and measles as well as in all children lacking in vigor but with no tangible disease.

An excellent explanation of the action of this fresh air on the body functions was made by Howland and Hoobler, who published the results of a series of experiments on children with pneumonia and tuberculosis at Bellevue Hospital, when they reported that they found a marked increase in blood-pressure from putting the children outdoors and an equal diminution in blood-pressure when the children were returned to the closed wards of the hospital. This seemed so rational an explanation that it was generally accepted and hardly seemed to need confirmation, but although several years have elapsed, no confirmation of these results has been published so far as I know.

In work done under the writer's supervision at the New York Foundling Hospital and at the New York Nursery and Child's Hospital by Dr. Schloss no corroboration of these results could be obtained, while at The Roosevelt Hospital, Dr. Hartshorn has carried out a considerable series of blood-pressure experiments, with no constant results. We are thus unable to confirm the results of Howland and Hoobler.

While some children have shown a considerable increase in blood-pressure on being put outdoors, others have shown no increase, while on the other hand, there has been no constant fall of blood-pressure noted in returning the children to the ward. In fact, we find that the blood-pressure, on the average, is no higher outdoors than in the ward.

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Pneumonia of infancy is a disease of housing. It has little tendency to develop in summer and is rarely found in winter in children that are kept in the open air. While for the cure of the disease an agent that is more efficient than any drug or serum or vaccine that is available at present is the freely moving outdoor air, and bronchitis and croup are no contra-indication to the use of this method of cure. A laboratory worker, Dr. A. W. Williams, after reviewing the various methods of treating pneumonia in the *Monthly Bulletin* of the New York City Board of Health, closes her article as follows: "Hygienic treatment, in which absolute rest and free exposure to the outdoor air is the main reliance, seems of late years to have greatly reduced the death-rate, and, until specific therapy is upon a sure footing, will remain the method of choice with most clinicians."

I have been able to carry on some interesting experiments in fresh-air treatment in The Roosevelt Hospital.

The Medical Pediatric Division of The Roosevelt Hospital consists now of a ward of eight beds, a quarantine ward of four beds, and a roof, partly covered by a shed and enclosed on the north, east, and west sides, with seven beds. They all are on the same floor and adjacent to each other, an arrangement that lends itself well to fresh-air treatment.

The bedsteads are painted with white enamel, which is not injured by dampness or wet, and are thus well adapted for this purpose. Ample bedclothes are provided for use in cold weather, as well as sufficient appliances, such as hot-water bags or heaters to keep the extremities warm. Mitts may be needed on the hands, while in very cold weather a cap for the head is desirable. The children are kept on the roof, not for a few hours each fine day, but day and night during all weather. Care is taken, particularly by feeling the feet, to see that the children are comfortably warm; they are brought into the wards only to be changed, bathed, or dressed.

An advantage of such outdoor treatment is the marked lessening of communicability. We have had cases of measles develop on our roof which were followed by no subsequent cases evidently due to these cases. This is an experience rarely met with in hospital wards.

Ten years ago a good deal was written concerning this outdoor treatment of hospital cases, particularly by Dr. Northrup, and while the results obtained continued satisfactory, this method of treatment has gradually fallen into disuse. Moreover, the application of this treatment has usually not been very thorough. A child would be kept outdoors a certain number of hours each day, but rarely have they been kept outdoors all the time.

The conditions which have seemed in our service to be most benefited by this fresh-air treatment are pneumonia, tuberculosis,

anemia, chorea, marasmus, and convalescents from any disease. Kidney and heart cases we have thought best to keep in the wards, although one child that had nearly died with endocarditis and pericarditis seemed during convalescence to have been much improved by living on the roof in winter, and this was allowed at his request, and was apparently much enjoyed by him.

I wish particularly to emphasize the fact that our wards are kept cool and well ventilated, so that any comparison between the ward and the roof is a comparison between a fairly open ward and a roof-shed.

The one disease that is most generally accepted as benefited by fresh-air treatment is pneumonia.

The method of treating these cases in The Roosevelt Hospital has been to give them an initial dose of castor oil, put them in beds on the roof, keep their extremities warm and their bowels open. Very few of the cases have received any stimulant or expectorant. In some cases when the cough was troublesome a dilute solution of tincture of chloride of iron in glycerin or water has been used.

Before considering our results of treatment of these pneumonias it will be of advantage to arrive at some idea of the mortality of pneumonia in children. Osler states that the mortality from bronchopnuemonia in children is 50 per cent. Holt gives a mortality of 5 per cent. for lobar pneumonia, but from bronchopneumonia in private practice from 10 to 20 per cent.; in uncomplicated bronchopneumonia in institution children of 50 per cent. and in complicated pneumonia of from 80 to 100 per cent., while classifying them by age he gives as the mortality of 346 cases during the first year, 66 per cent.; second year, 55 per cent.; third year, 33 per cent.; fourth year, 16 per cent. The mortality of the last 42 cases of lobar pneumonia at the New York Nursery and Child's Hospital, where conditions are very good, was 19 per cent., while that of the last 221 cases of bronchopneumonia was 33 per cent. In the New York Foundling Hospital, where the children are mostly under three years of age, the last 114 cases of lobar pneumonia showed a mortality of 32 per cent., while the last 736 cases of bronchopneumonia gave a mortality of 51 per cent. Of the last 108 cases of pneumonia treated at the Pediatric Service at The Roosevelt Hospital 21 were discharged as improved or unimproved, leaving 87 that remained to the termination of the disease. Of these 87 cases 25 were lobar pneumonia and 62 were bronchopneumonia. Of the 25 cases of lobar pneumonia three died, giving a mortality of 12 per cent., while of the 62 cases of bronchopneumonia 16 died, giving a mortality of 21 per cent.

Many of these cases were complicated: one turned out at autopsy to be tuberculosis, and in others death really was precipitated by other diseases. Perhaps the best estimate of our results is obtained by considering our uncomplicated cases of pneumonia: The 21

cases of uncomplicated lobar pneumonia showed one death in a child of six months, giving a mortality of 4.7 per cent., while the 31 cases of uncomplicated bronchopneumonia showed only one death in a child of nine months, giving a mortality of 3.3 per cent.

These uncomplicated cases of bronchopneumonia ran an average course after admission of seven days, and the cases of uncomplicated lobar pneumonia ran an average course after admission of three days.

One case of particular interest was that of a colored boy, aged five years, who came into the hospital with typhoid fever. He ran the ordinary four weeks' fever, followed by a relapse of two weeks, at the end of which time, after having been in the ward eight weeks, he developed pneumonia and was immediately put on the roof. The pneumonia involved first the right upper lobe, then the left lower and the right middle lobe. The breathing was bronchial on the right side, and soon we found developing on our Röntgen-ray plates two cavities in the right middle lobe. These became larger, the sputum became foul, and physical signs of these cavites developed. The boy was desperately sick for a long time, but was finally discharged eighteen weeks after admission, with a practically normal temperature. He has since made a good recovery and has been at school during the past winter. This boy would, I believe, have certainly died if he had not been put on the roof.

Recently he has been returned to our ward with signs of consolidation over the right middle lobe, with a Roentgen-ray plate that shows the presence of the old cavities with consolidation in the neighborhood, and areas that are fairly typical of tuberculosis. He was running a moderate temperature, with marked remissions, and was vomiting on admission. During the days he has been on the roof his temperature has become more moderate, he has stopped vomiting, his appetite has improved, and his last roentgenogram shows a marked clearing of the areas of consolidation in his lungs.

Perhaps our most interesting results of the roof treatment have been in the cases of abnormal conditions of the blood. One simple anemia made a wonderfully speedy recovery, with little medicine and roof treatment.

A poorly nourished child, aged thirteen months, came to our service running a considerable temperature of from 101° to 103°, with bronchitis, gastro-enteritis, and a marked simple anemia. The hemoglobin was only 22 per cent.; red cells, 2,840,000; white cells, 7700. There was moderate poikilocytosis and anisocytosis (Chart I).

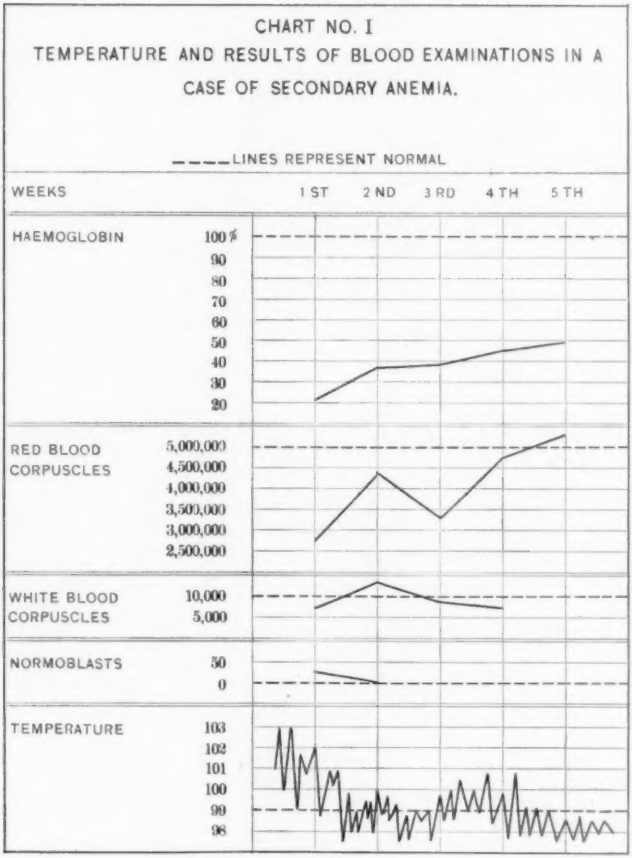
This child was given seven drops of syrup of iodide of iron three times daily in addition to the treatment on the roof. The improvement was very rapid, the temperature in a week having reached normal, while in four weeks from admission the hemoglobin was 45 per cent., and the red cells 5,030,000. The weight had increased

one pound. The respirations had fallen from 38 to 29. The pulse had dropped from 136 to 100. The rapid improvement of this child is well shown on Chart I.

A very marked case of von Jaksch's anemia occurred in a colored child, a Porto Rican, aged three years. The child complained

CHART NO. I

TEMPERATURE AND RESULTS OF BLOOD EXAMINATIONS IN A CASE OF SECONDARY ANEMIA.



of fever and headache, had a large spleen, and ran a temperature of 102° for ten days after admission. She was put on the roof and was given no medicine excepting such as might have been necessary to keep her bowels open. Her blood count on admission was: Hemoblogin, 17.5 per cent.; red blood cells, 1,368,000; index,

0.77; white blood cells, 41,000; polynuclears, 74 per cent.; lymphocytes, 26 per cent.; megaloblasts, 10; anisocytosis and poikilocytosis. The blood count showed a markedly typical von Jaksch's anemia condition.

Eight days later the blood had improved, as shown on Chart II. The next week showed still further improvement, the normoblasts and megaloblasts having nearly disappeared, while on April 29 the child was so well that she was discharged, the spleen, however, remaining large.

Six weeks later the child returned with pneumonia, the blood, however, being much the same as when the child was discharged, showing none of the changes characteristic of von Jaksch's anemia. The child made a recovery on the roof from pneumonia and was not seen again until last January, when she came in with the following blood count: Hemoglobin, 25 per cent.; red blood cells, 1,600,000; index, 1.1; white blood cells, 50,000; polynuclears, 70 per cent.; lymphocytes, 27 per cent.; myelocytes, 3 per cent.; normoblasts, 48; megaloblasts, 18. Anisocytosis and poikilocytosis. Red blood cells: largest, 12.6 m.; smallest, 2.1 m.

The spleen remained about the same size. Normoblasts and megaloblasts were present in considerable numbers, and there was a considerable increase in the number of white cells and a diminution in the red cells.

One week on the roof almost eliminated the normoblasts and megaloblasts and brought the white cells down to normal. At that time it occurred to me that the improvement in the child's condition might not be due to the roof treatment but might be due simply to hospital care. Therefore on January 20 the child was put in the ward. The temperature immediately began to rise, and although we had contemplated leaving the baby in the ward for a week, on the sixth day the child was doing so badly it was felt that it was not fair to leave her there any longer, and she was taken to the balcony. At that time the blood had changed as follows: Hemoglobin, 33 per cent.; red blood cells, 1,600,000; index, 1.2; white blood cells, 17,400; polynuclears, 60 per cent.; lymphocytes, 32 per cent.; myelocytes, 8 per cent.; megaloblasts, 4.

After a week on the balcony there was a marked improvement in the blood count, as indicated below: Hemoglobin, 36 per cent.; red blood cells, 2,400,000; index, 0.9; white blood cells, 14,400; polynuclears, 56 per cent.; lymphocytes, 35 per cent.; myelocytes, 0; normoblasts, 2; megaloblasts, 1.

During this time the child's temperature returned to normal, but, unfortunately, she showed gonococci in a vaginal smear and had to be transferred.

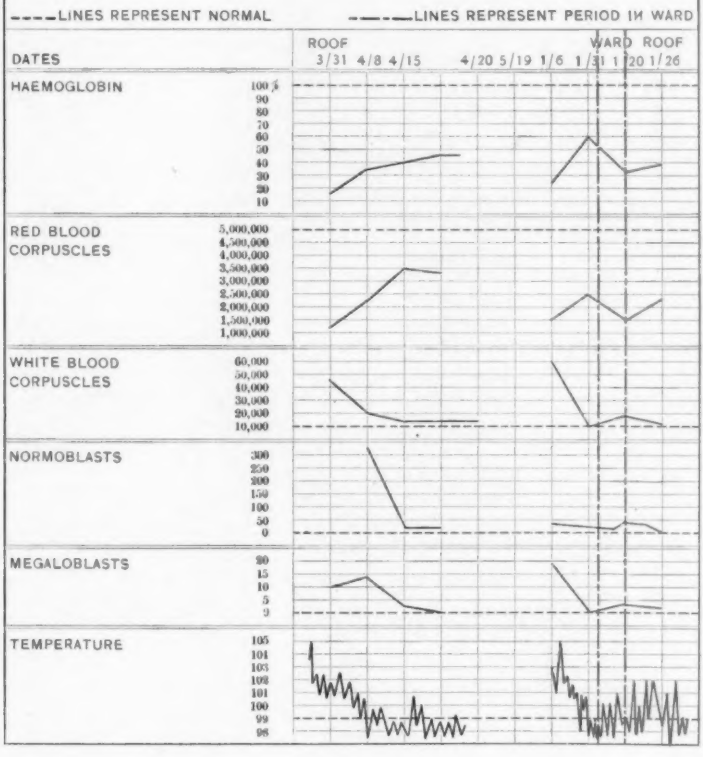
Chart II shows well the approach to normal of the abnormal condition of the blood as well as the lowering of the temperature while on the roof; the return toward the original condition on

admission during the six days in the ward, and the subsequent improvement on the roof.

A third child, aged four years, of French and German parentage, a case of leukemia, gave a history of cough for four months, swelling

CHART NO. II

TEMPERATURE AND RESULTS OF BLOOD EXAMINATIONS IN A CASE OF VON JAKSCH'S ANEMIA.



of the neck for four weeks, dyspnea, constipation, pains in legs and arms, anorexia, and fever for a few days. He had dysentery when six months old. His complexion had always been yellow.

Physical examination showed a fairly well-developed boy, with skin so dark as to suggest mulatto blood. He was evidently

anemic and looked sick. There was slight dyspnea, with inspiratory stridor and slight cough. The tongue was moist and clear. The teeth were decayed. There was a general enlargement of the lymph glands all over the body. The parotid and submaxillary glands were markedly enlarged but not tender, while large masses of lymph nodes filled up the neck. Large groups of lymph nodes were in both axillæ, extending out over the anterior chest wall. The epitrochlears were felt, and the inguinal glands were markedly enlarged. The chest showed a diminished excursion on the left

FIG. 1.—The child with leukemia, showing lymph-node enlargement indicating the lower border of the liver as well as the outline of the spleen.

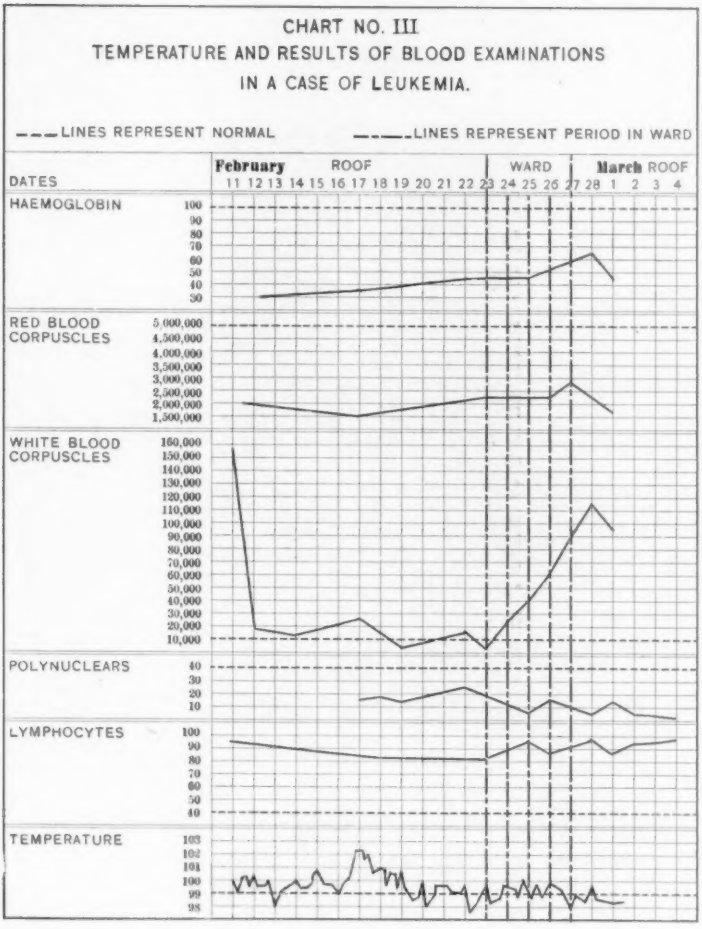
side. There was on the same side some dulness, with, however, a rather tympanitic note over the scapula. There were a few moist rales on this side, with diminished breathing of a somewhat bronchial type. The abdomen was large, showing a markedly enlarged liver and spleen, as indicated in the sketch (Fig. 1), the spleen extending seven and one-half inches below the free border of the ribs in the mammary line and one and one-quarter inches to the right of the midline at the navel.

The blood count showed: hemoglobin, 30 per cent.; red blood

cells, 2,000,000; white blood cells, 158,400; neutrophiles, 2 per cent.; basophiles, 1 per cent.; small lymphocytes, 5 per cent.; large lymphocytes, 90 per cent.; turik irritation, 2 per cent.; anisocytosis and poikilocytosis.

CHART NO. III

TEMPERATURE AND RESULTS OF BLOOD EXAMINATIONS IN A CASE OF LEUKEMIA.



The Roentgen-ray plate showed a consolidation of practically all of the left lung, while an exploratory puncture of the left chest withdrew a few drops of turbid amber fluid.

This child was placed on the roof where, as may be seen by Chart III, the white cells dropped in twenty-four hours from 158,400 to 15,000. The general appearance improved and the child began to get color in his cheeks. Each Roengten-ray plate showed further

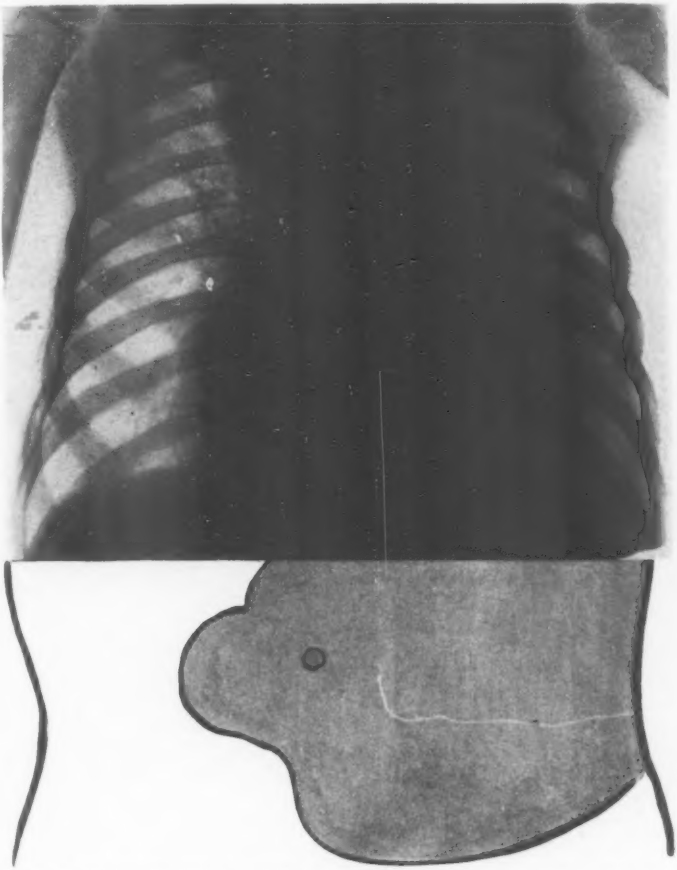


FIG. 2.—Leukemia case on admission, showing size of spleen and shadow in left lung.

clearing up of the pneumonia and physical examination showed a diminution in the size of the spleen, so that on the thirteenth day after admission all the lymph nodes as well as the salivary glands having diminished in size, the spleen having contracted from seven and one-half to four and one-half inches below the free border of the

ribs and no longer coming forward to the median line, a considerable portion of pneumonia having cleared up, as shown by the Roentgen-rays, and the blood having a normal number of leukocytes and being improved in other respects, the child was put in the ward. In this ward during a considerable part of the time that the child was in

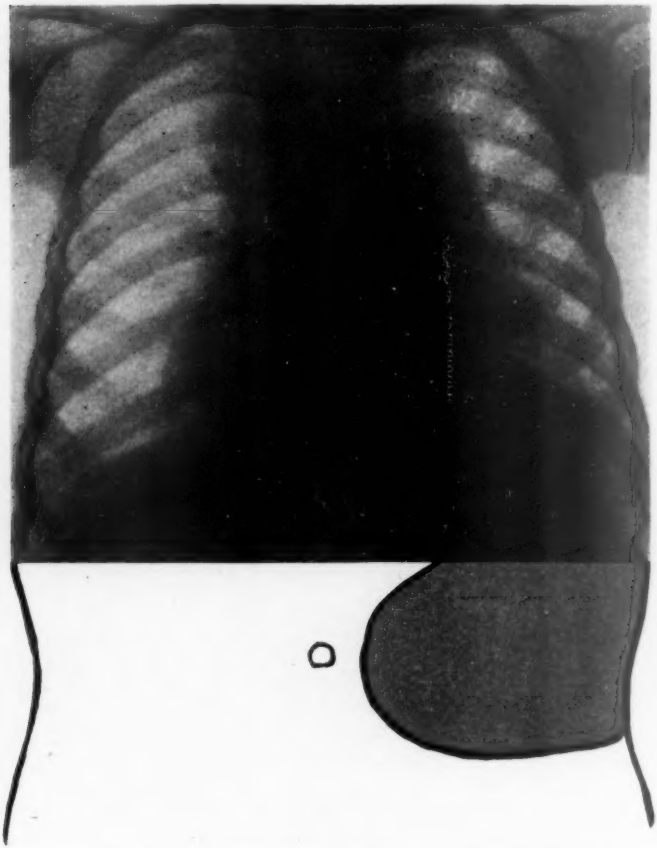


FIG. 3.—Leukemia case after twelve days on the roof, showing diminution in shadow made by left lung and diminution in size of spleen.

it, the windows at both ends were open and it was always well ventilated.

At the end of four days in the ward the lymph nodes were as large as they were on admission. The spleen had again extended beyond the median line, and to seven and one-half inches below

the free border of the ribs. The leukocytes, which had been daily increasing, had reached again 90,000, so that it seemed unfair to keep the child longer under these conditions, and he was again removed to the roof. Fig. 3 shows well the diminution in the shadow made by the left lung and the diminution in size of the

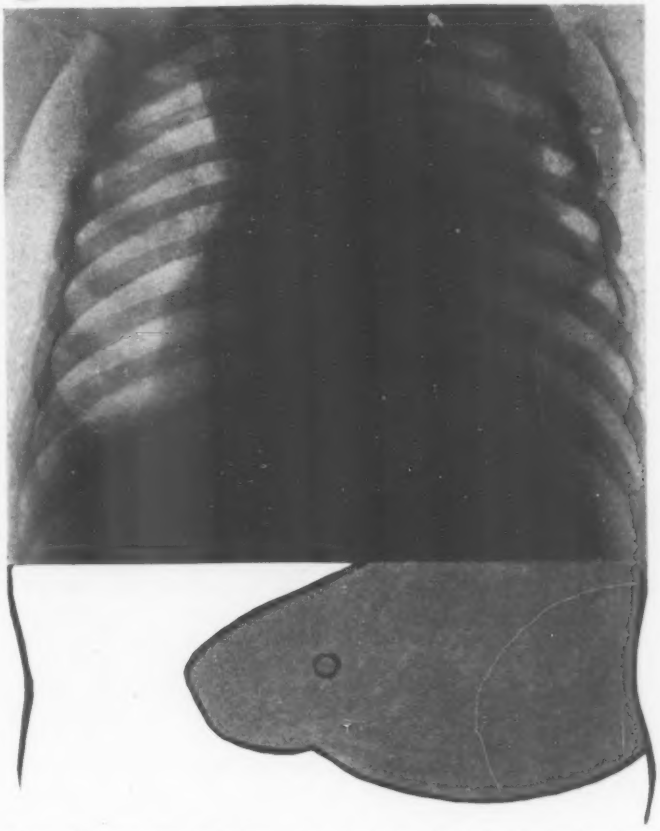


FIG. 4.—Disastrous effect on leukemia case of only four days in a well-ventilated ward.

spleen after the patient had been on the roof twelve days, while Fig. 4 shows the disastrous effect of only four days in a well-ventilated ward.

It is, of course, evident that three cases of sickness associated with abnormal conditions of the blood are not sufficient for drawing any conclusions, but in at least two of these cases it does seem as

if a fairly reliable demonstration of the influence of fresh air alone had been made.

SUMMARY. Treatment of children in an open-air shed in winter increases their vitality and resistance to disease more powerfully than medicines.

Pneumonias run a short course and show a very low mortality Certain abnormal conditions of the blood will rapidly improve with little or no medical treatment.

A PRELIMINARY REPORT ON PNEUMONIA IN CHILDREN, WITH SPECIAL REFERENCE TO ITS EPIDEMIOLOGY.[1]

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THE importance of pneumonia as a cause of death is hardly to be exaggerated. According to the United States census of 1900, pneumonia accounts for 3 per cent. of all diseases, with a mortality rate of 6.6 per cent., or of 12.7 per cent. if only medical cases are considered. It averages not less than 1.5 to 2.3 deaths per 1000 persons living. If pneumonia may be called the "old man's friend," it is just as certainly the enemy of youth, and especially of infancy. During early life the most common seat of organic disease is the lung, and some form of pneumonia is a large—perhaps the largest—factor at the present time in infant mortality. It is perhaps the only infectious disease in which the etiological cause supposedly is well understood whose incidence and rate have not been affected by such knowledge.

It is a matter of reproach to the profession that one hundred years of progress and varied methods of prevention and treatment have not affected the mortality rate of pneumonia in either adults or children.

The importance of pneumonia as a disease of infancy is well illustrated from the following mortality table of 1000 cases, which covers a period of the last nine years in the Babies' Wards of the New York Post-Graduate Hospital. The children were all under six years of age.

[1] Read at the Annual Meeting of the American Pediatric Society, May, 1915.

TABLE I.—1000 CASES OF PNEUMONIA FROM THE BABIES' WARDS OF THE NEW YORK POST-GRADUATE HOSPITAL.

		Per cent.
Cured	513	51.3
Dead	343	34.3
Improved	62	6.2
Unimproved	15	1.5
Termination not known	4	0.4
Transferred	63	6.3
Total	1000	100.0

That this mortality rate is not excessive is shown by a death rate of 33.1 per cent. obtained from a series of 410 cases collected by Holt.[2] Holt's series included 223 cases of bronchopneumonia and 187 cases of lobar pneumonia in children. The age incident is apparently about the same in the two series. Pneumonias secondary to infectious diseases, such as whooping cough, measles, etc., are not included in either group of cases.

Pfaundler has made the observation that children are ill of nutritional disturbances, but that they die of infection. The truth of that statement is supported by 84 of our cases of pneumonia, which were frankly secondary to other disturbances, with a mortality rate of 52 per cent. Of these 84 cases, 24 occurred as a complication of malnutrition, rickets, and enteritis, with a death rate of 62.5 per cent.

From the clinical stand-point, pneumonia seems naturally to fall into two groups, namely, (1) bronchopneumonia, and (2) lobar pneumonia. The differentiation between the two types is important from the stand-point of prognosis, of treatment, and of prevention, and undoubtedly could and should be made more frequently. It is proposed tentatively to prove that the two conditions of bronchopneumonia and lobar pneumonia are not identical either pathologically or bacteriologically.

Bronchopneumonia undoubtedly occurs as a primary condition, but most frequently is secondary to other diseases, such as bronchitis or a moderate or severe intestinal disturbance. A large percentage of the cases in children occur during the first two years of life, though it may occasionally be met with at any age. Of 415 cases treated in the Babies' Wards of the Post-Graduate Hospital during the first three years of life, 41 per cent. died. In the following table it will be noted that the number of cases of bronchopneumonia rapidly diminishes after the second year, so that in this series of 1000 cases, of which 445 were bronchopneumonia, there are only 31 cases of bronchopneumonia between the ages of four and six years. In other words, of 445 cases of bronchopneumonia, 414 were infections of the first three years of life, and more than half of all the cases in this group occurred during the first year.

[2] Diseases of Infancy and Childhood, 6th ed., pp. 515–535.

TABLE II.

	Post-graduate cases.		Holt's cases.	
	Cases.	Mortality, per cent.	Cases.	Mortality, per cent.
During the 1st year	226	52.2	202	66.0
" 2d year	155	29.0	102	55.0
" 3d year	33	24.2	33	33.0
" 4th year	13	0.0	6	16.0
" 5th year	13	0.0	3	0.0
" 6th year	5	0.0		

Of the lobar pneumonia cases there were 227, and they are fairly evenly distributed throughout the first six years, though the first and second years include more than half the total number. It will be noted that the mortality rate is distinctly lower than for bronchopneumonia, being for the entire six years 28.1 per cent. If the first two years of high mortality are eliminated the death rate falls to 10.8 per cent.

In the following table is seen the incident of mortality by age in 227 cases of lobar pneumonia studied:

TABLE III.—LOBAR PNEUMONIA.

	Cases.	Mortality, per cent.
During 1st year	75	40.2
" 2d year	97	34.0
" 3d year	31	12.9
" 4th year	25	16.0
" 5th year	21	0.0
" 6th year	14	0.7

Judging from this series of 1000 cases of pneumonia, empyema is not a frequent complication. In all there were 41 cases, or 4.1 per cent., of empyema, of which 5 followed bronchopneumonia, the other occurring as a complication of lobar pneumonia.

Pathologically, it is questionable whether empyema ever occurs in a true case of bronchopneumonia. Wollstein and Meltzer,[3] in experimental bronchopneumonia on dogs, by means of intrabronchial insufflation, found practically complete absence of pleurisy in 20 experiments, while in true lobar pneumonia there was always a definite pleurisy even in non-fatal cases. Consequently, there must be some questioning of the 5 cases in this series which appear as a complication of bronchopneumonia. A few cases of empyema due to streptococcus have been reported, but the only case which has come directly under our observation was one of Streptococcus hemoliticus, occurring as a complication of an undoubted lobar pneumonia due to the pneumococcus.

It should be added that these 41 cases include only those empyemas which occurred as a complication of a pneumonia treated in the wards, and consequently have no relation to the total number of empyemas admitted to the hospital.

[3] Jour. Exper. Med., 1912, xvi, 126.

In a study of groups of pneumonia by months it may be easily shown that the mortality rate at certain times is unusually high, as, for instance, during January and February of 1915. The large number of cases which were fatally ill during these months, which was much higher than for corresponding months of other years—in fact, was the inspiration for the special bacteriological study—the results of which are detailed in this paper.

The most obvious explanation for the variation of the mortality rate of pneumonia from year to year and from month to month is found in a difference in the virulence of the pneumococcus, a highly virulent organism resulting in many deaths and extraordinary severe pneumonias; an organism of low virulence, on the other hand, giving an infection in which recovery is the more common outcome.

Opposed to the argument that pneumonia arises when organisms of increased virulence reach the lung is the fact that pneumonia rarely occurs in epidemics. A few such epidemics, however, have been described, the most widely advertised of which occurred in Panama during the first year of the American occupation, and the one in South Africa, which reached such proportions as to seriously menace the working of the mines. Curschmann[4] describes an epidemic which was supposed to be due to influenza, in which cultures showed, in 49 cases, pneumococci in almost pure culture. The organisms were highly virulent for mice, and presented other characteristics of pneumococci. Leeds[5] describes another such epidemic in which a most careful search for the influenza bacillus was completely negative and the infecting organism was unquestionably the pneumococcus. A careful scrutiny of our cases fails to reveal any evidence of an epidemic or even of a house infection. In 50 cases very carefully studied from all stand-points there is only 1 case in which the pneumococcus was apparently transmitted from a twin sister, and in this instance the type was that of a bronchopneumonia.

Cole,[6] following the method of Lamar and Meltzer, of bronchial insufflation with broth cultures of various strains of pneumococci, has been able to prove that in rabbits, at least, the production of lobar pneumonia is somewhat dependent on the race of organisms used. A pneumococcus having a very slight virulence may end in a recovery of the animal without lung lesions, while if the organism is too virulent the animal quickly succumbs to a septicemia, and at necropsy shows only a congestion and edema of the lungs. Lamar and Meltzer[7] were the first to regularly produce a lobar pneumonia in animals, though Wadsworth,[8] eight years earlier, by

[4] Münch. med. Wchnschr., 1909, lvi, 377.
[5] Ztschr. f. Hyg. u. Infectionskrankh., 1912, lxxi, 3.
[6] Arch. Int. Med., 1914, xiv, 8.
[7] Jour. Exper. Med., 1912, xv, 133.
[8] Amer. Jour. Med. Sci., 1904, cxxvii, 851.

carefully balancing the general resistance of the animal with the virulence of the race of pneumococci employed, and by injecting the organism intratracheally, produced in a series of rabbits a diffuse exudative inflammation like the acute lobar pneumonia seen in man.

Wollstein and Meltzer by the use of other organisms, such as streptococcus and influenza bacillus, produced on all occasions a diffuse lesion which resembled closely that seen in bronchopneumonia.

An important factor in the production of pneumonia in animals is the number of organisms which are used. Even in susceptible animals a considerable number of virulent organisms is necessary to produce an infection. Gillespie[9] carried on some important experiments which have a bearing on this problem of why, when a considerable number of virulent organisms is injected, there is multiplication and infection, while if only a few organisms are injected they fail to multiply. It has long been recognized that in starting a culture of pneumococci in broth the number of organisms used depends upon the amount of culture media. For instance, an ordinary loopful of pneumococci might be sufficient to start a growth in 10 c.c. of bouillon, and result in failure if a liter of bouillon were used. Even on serum agar the growth is more rapid and profuse if a stab into the culture is made and the smear started from this point. If the culture is made in a solid media, one organism probably produces a colony. Gillespie was able to show that if the inoculation were made on filter paper kept constantly wet by bouillon, a growth would occur with an inoculation of as small a number of organisms as is required in agar and with a much smaller number than is required to inoculate the bouillon. The conclusion was drawn that for growth to occur the pneumococcus must change the medium immediately surrounding it, and that where diffusion is great the local changes cannot be kept sufficiently constant unless there is a considerable number of organisms in close proximity. This observation has an important bearing on the production of pneumonia. It is not considered that in order to produce pneumonia any such number of pneumococci must be introduced into the infantile being as was necessary to cause a pneumonia in the animals experimented upon by Lamar and Meltzer, but it does appear to be reasonable to suppose that if by any process a few of the terminal bronchioles are occluded, forming a small closed cavity, that pneumococci would be in a situation favorable for their multiplication. According to Cole,[10] extension of the process apparently takes place, in adults, at least, from one lobe to another through the bronchi, as the study of large sections through lobes with beginning involvement shows. It is common knowledge that

[9] Jour. Exper. Med., 1913, xviii, 584.

[10] Loc. cit.

pneumonia in children in a large number of instances follows after a few days of coryza, cough, and not infrequently a bronchitis. It may well be that conditions of this nature, extending along the bronchi, produce a favorable environment for the growth of pneumococci, which, as may be seen from the following table, are so frequently present in the upper respiratory tract of children.

TABLE IV.—PLATE CULTURES OF NON-PNEUMONIA CASES SHOWING TYPES OF ORGANISMS PRESENT.

	Age.	Pneumococcus.	Streptococcus (hemolytic).	Streptococcus viridans.	Staphylococcus.
Regulation of diet	4 mos.	.....	++	.....	+
" "	2 mos.	*	++	.....	+
" "	14 wks.	+	.....	+	+
" "	16 mos.	.....	++	.....	+++
" "	7 wks.	.....	.....	.....	+++
" "	.....	*	.....	.....	++
" "	1 mos.	.....	.....	.....	+++
" "	.....	.....	+	+++	+
" "	4 mos.	.....	.....	.....	++
" "	10 wks.	.....	++	.....	++
" "	4½ mos.	*	.....	.....	++
" "	5 wks.	*	++	.....	+
Malnutrition	3 mos.	.....	++	.....	+
Tertian malaria	12 mos.	.....	++	.....	+
Hypertrophied tonsils and anemia	31 mos.	.....	+	.....	++
Acute intestinal toxemia	2½ yrs.	.....	+	.....	++
Tuberculous peritonitis	24 mos.	+	+++	.....	+
Chronic endocarditis	5 yrs.	+	+++		
Regulation of diet	12 mos.	.....	+++		
Empyema	3½ yrs.	+	+++	+	
Pneumonia	4½ yrs.	++	+		
Rickets	1½ yrs.	.....	+	.....	+
Otitis media and rickets	22 mos.	+	++	.....	+
Pyelonephritis	24 mos.	.....	.....	++	
Hospitalism	4 mos.	++	+	.....	+
Eczema	15½ mos.	.....	++	.....	+
Von Jaksch pseudoleukemia	3 yrs.	+	+	++	

The table shows the results of plate culture of sputum in blood agar. Where necessary the pneumococcus findings were verified by inoculation into mice, but, as a rule, the color of the colony, the morphology, and the action of bile upon the organism served to identify it. The specimen was nearly always taken from the upper part of the larynx with a bent applicator. In addition to this series, in which the lung, with one or two exceptions, was free of any known lesion, smears were made from 23 cases of lobar pneumonia in which the sputum was virulent for mice. In all of these a Gram-positive diplococcus was found, and in nearly ever case it was the predominating organism, with a few scattered streptococci and staphylococci. In 10 cases of mild bronchopneumonia, the sputum of which did seem to be virulent for mice, the predominating organism was in 5 cases streptococcus; 2 cases each of staphylococcus and influenza bacillus; and in 1 case, tuberculosis bacilli with other organisms.

A few pneumococci were found in four of the series of bronchopneumonia studied, and it is possible that if a larger or more char-

acteristic specimen found could have been obtained that the sputum would have been found virulent for mice.

There were 8 cases of bronchopneumonia in which the sputum was virulent for mice, and in all of these a large number of pneumococci were found in the smears. There were, in addition, however, many other organisms, chiefly of the streptococcus and staphylococcus groups, so that these infections could be fairly labelled as mixed infections. These findings would explain in a measure the difference between a bronchopneumonia and a lobar pneumonia—the bronchopneumonia being a mixed infection, or an infection chiefly with a single type of organism other than the pneumococcus. For this reason the inflammation is peribronchial in character and consists primarily of an infiltration of interstitial tissue with leukocytes. The exudate into the alveoli is moderate and contains little or no fibrin. In lobar pneumonia the inflammation is due chiefly or entirely to the pneumococcus and is not peribronchial in character, and the framework of the lung is free of infiltration. The exudate is considerable and contains a large amount of fibrin. According to Wollstein and Meltzer, slightly virulent or non-virulent pneumococci produce an exudate that resembles that of a virulent streptococcus in the small amount of fibrin present in the exudate.

The question naturally arises as to why infection occurs at all. It has just been shown that pneumococci were found by cultural methods in approximately 25 per cent. of the throats of small children examined in a routine manner in our wards (lungs free). There is no evidence to show that the organisms normally in the throat differ from those which cause pneumonia. There is considerable evidence that different races of pneumococci vary in their virulence toward animals. But the fact remains that some of these organisms which have little virulence for animals have been recovered from cases of severe pneumonia. Whether the resistance to pneumococci has temporarily been lowered in these patients sick with pneumonia is a speculative question to which no reply has apparently been made. It may be believed that the infection is the result of a combination of circumstances, such as the natural or acquired resistance of the individual, the state of the vitality of the individual, local changes in the respiratory tract which precede the infection, and, finally, the virulence of the organism.

Dochez and Gillespie,[11] in their important study, have been able to show that the pneumococcus is a family, which, by the extraordinarily specific methods developed from the study of immunity, can be subdivided into many races having varying degrees of virulence. They liken their subdivision of the family of pneumococcus to other grosser methods of classification, such as differ-

[11] Jour. Amer. Med. Assn., 1913, lxi, 723.

ences in growth or cultural characteristics that are sufficient in certain groups of organisms for differentiation. From the etiological stand-point they do not consider these fine lines of division as important, but from that of specific therapy these differences are of primary importance. At the Rockefeller Institute, under the direction of Dr. Cole, they began in 1910 to use an immune serum that was prepared by injecting a horse with a culture of pneumococcus obtained from Professor Neufeld, the same race he had used in the production of his immunized serum. The protective power of this serum for mice was found by Dochez[12] to be effective in only about one-half the cases. A biological classification of pneumococci was then undertaken by Dochez and Gillespie.[13] Rabbits were immunized to each race of pneumococci, and the protection afforded by these different rabbit serums against all other races of pneumococci was determined.

A considerable number were found to show cross-protection, that is, a serum prepared by injections of one of the number acted on all the races of this group. A horse was then immunized to one of this group and the serum was called Serum No. 2. In this way the pneumococci obtained from all cases of pneumonia were separated into four groups.

Group I contains all those races against which Serum No. 1 is effective.

Group II contains all those races against which Serum No. 2 is effective.

Group III consists of all the organisms of the so-called Pneumococcus mucosus type. The individual organisms show a voluminous capsule containing medium-sized, closely approximated cocci with definitely round ends. They produce a sticky exudate in animals and on solid media a moist, transparent mass.

Group IV includes all the cases against which Serum No. 1 and Serum No. 2 are not effective and which from their other properties do not belong in Group III. This group seems to consist of entirely isolated individuals, the significance of which it is difficult to interpret according to Dochez. It may be that this heterogenous group may be representative of the type of pneumococcus found in the normal mouth.

In our experiments there were obtained eleven strains of pneumococci from the throats of children having no lung involvement all of which belonged in Group IV. In one case pneumococci of Group I were obtained before physical examination revealed a lobar pneumonia.

The chief difficulty met with in babies and small children was the obtaining of a sufficient specimen for a direct mouse injection. The method which was finally adopted was a simple one, con-

[12] Jour. Exper. Med., 1912, xvi, 680.
[13] Jour. Amer. Med. Assn., 1913, lxi, 727.

sisting of a tongue depressor, placed well back on the tongue and down in the throat. This method resulted in some gagging and more or less coughing, which in most cases brought a plug of mucus up into the throat, which was caught on the spatula. While the amount obtained was often scanty, only occasionally was it necessary to take a second or a third specimen. The method used from this point closely follows Dr. Cole's description of the method used at the Rockefeller Institute. The sputum was immediately injected into the peritoneal cavity of the mouse. The pertoneal cavity was washed with salt solution as soon as the mouse showed symptoms of being severely ill. The cells were thrown down in a centrifuge, a suspension of the organisms being thus obtained. The agglutination test was at once made with Serum No. 1 and Serum No. 2.

At the same time that this was being done a very small amount of blood was withdrawn from the heart and smeared across a blood-agar plate. In twenty-four hours the type of colony can be studied on the plates and further agglutination or cultural tests made. The work was checked by a Gram and a capsule stain (His's method) and by lysis of the bacteria with bile. In making the agglutination tests from the peritoneal washings the amount used depended somewhat upon the opacity of the solution containing the suspension, and 0.3 c.c. of the serum was the amount employed.

Our final test was always made with an eighteen-hour-old broth culture inoculated from typical plate colonies. Equal amounts of the broth and serum were employed in the test (as a rule, 0.3 c.c. broth culture and 0.3 c.c. of serum). It was noted that a fairly high dilution of the serum often made it difficult to obtain an agglutination; but, as a matter of fact, the organisms seem to have the property of remaining suspended in the serum used, even though the serum was not diluted at all. Readings were made macroscopically at the end of one and two hours at 37° C., and again after standing twenty-four hours in the ice-box. Usually, agglutination was visible in fifteen minutes or half an hour, and consisted at first of a fine granulation followed by a sinking of clumps which form a thin layer on the bottom of the tube that could not be broken up even by vigorous shaking.

The serum for Groups I and II was obtained through the kindness of Dr. Cole, at the Rockefeller Institute. Somewhat to our surprise, for we expected many of our pneumonias to fall into Group IV, our cases paralleled quite closely those at the Rockefeller Institute so far as groups are concerned. We obtained many more in Group II than Dr. Cole's published results would seem to warrant; but in a personal communication, Dochez has told us that he too had an unusually large number of organisms fall into Group II during the past winter. The following table briefly summarizes our results:

	Cases of lobar pneumonia.	Cases of broncho-pneumonia.	Primary.	Secondary.	Deaths.	Cures.	Total number of cases.	Percentage in each group (cases with no results not included).	Per cent. of mortality.
Group I	9	2	9	2	1	10	11	22.9	9
Group II	11	3	12	2	5	9	14	29.3	36
Group III	1	3	2	2	1	3	4	8.3	25
Group IV	7	12	6	11	4	15	19	39.8	21
No result	3[14]	12	..	..	..	..	23[15]		
Total	...	..	..	..	..	..	71		

It will be noted that there are 48 cases in which it has been possible to determine the group to which the pneumococcus causing the infection belongs. Of the 23 cases in which it was not possible, for one reason or another, to obtain a pneumococcus culture, in at least 3 a positive result would in all probability have been obtained with a proper specimen. Empyema occurred as a complication in 7 of these cases. With one exception, the organism recovered from the empyemas was the pneumococcus, of which 2 belonged in Group I, 3 in Group II, and 1 in Group IV. The seventh case gave a pure culture of Streptococcus hemolyticus.

Our mortality-rate for the groups, with the exception of Group IV, is somewhat lower than in the series published by Cole.[16] For purposes of comparison, mortality percentages for the two series are placed side by side.

	Our series.	Cole's series.
Group I	9 per cent.	24 per cent.
Group II	36 "	61 "
Group III	25 "	60 "
Group IV	21 "	7 "

The number of cases in both series is as yet insufficient for the determination of the absolute mortality rate in each group. As our series is based on children under six years of age, a comparison with Cole's adult cases is obviously unfair. Lobar pneumonia decidedly predominated in Groups I and II, while rather more than half the cases in our Group IV were clinically bronchopneumonia, while the cases dealt with by Dr. Cole are exclusively of the lobar type. Moreover, there is an actual difference in the mortality-rate in the two series, ours being 23 per cent., as opposed to Dr. Cole's 38 per cent. In all probability this marks another difference in the two series, as we used every pneumonia case that came into our children's service, while probably only very ill patients were sent to Dr. Cole's service at the Rockefeller Institute.

SUMMARY. From a study of a thousand cases we have established a mortality-rate for pneumonia of 34.3 per cent. It is admitted that this is probably a higher rate than obtains in private practice

[14] Two cases sputum taken after all symptoms had disappeared.
[15] Eight of these were control cases, having no lung involvement.
[16] Loc. cit.

among well-to-do people, but is the average for the mass of city dwellers in this locality. Bronchopneumonia is preëminently a disease of the first two years of life, and after the third year is relatively uncommon. Lobar pneumonia is the type of the disease which is present after the third year in practically all cases of pneumonia, if those cases which are frankly secondary to some other condition, such as one of the infectious diseases, or where the pneumonia occurs as a terminal infection, are omitted. Lobar pneumonia *per se* is a common condition in the first and second years of life, being much more frequent than is commonly supposed. The infection which is the etiological factor of lobar pneumonia is always the pneumococcus, while a bronchopneumonia may be due to a number of organisms, such as the streptococcus or the influenza bacillus, occurring alone or as a mixed infection. If pneumococci are present in bronchopneumonia they are usually one of a group of various organisms, or at least are of a low virulence, and resemble the organisms commonly found in the mouth. The pneumococcus may be divided into four general groups, each being made up of many races which are closely related. By the method outlined a pure culture of pneumococcus may be obtained and the group determination completed in about twenty-four hours from any given case of pneumonia. The division of the pneumococcus into groups is of the greatest importance from the stand-point of treatment. Obviously the treatment of a lobar pneumonia due to a pneumococcus of Group II with a serum or vaccine prepared from an organism of Group I is a waste of energy and might be positively harmful in its effect.

Pneumonia is the most common, is the most fatal, and is the least studied disease that occurs among children. Any work which brings new facts relating to its treatment or new possibilities of improved methods and prevention is worthy of the careful consideration of all those who are interested in the welfare of children. It is hoped that the division of pneumonia into groups will eventually bring about the treatment by specific sera or vaccines, replacing the symptomatic treatment of today.

ACUTE CEREBELLAR ATAXIA IN CHILDREN: REPORT OF A CASE, WITH RAPID AND COMPLETE RECOVERY.

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The condition about to be described appears to be an uncommon one. On this account it seems well to put the following case on record and to review the already published cases of a similar nature.

Susie R., aged five years. The family history showed nothing of importance. There were three brothers and one sister, who were well. The patient had always been a healthy child, except for occasional attacks of bronchitis. There had been no illness of any sort in the household recently. On Monday, January 4, she suffered from cold in the head and a bronchial cough. An epidemic of influenza had been prevailing in the city. The symptoms continued upon Tuesday, January 5, although the child was running around as usual. On Wednesday, January 6, she was worse, and Dr. Wm. McCombs attended her for the next several days, and put her to bed. She had a heavily coated tongue, headache, and a temperature from 98° to 102°. She continued about the same from January 7 to January 9, when her temperature had become normal. By Sunday, January 10, she was apparently quite convalescent, and was allowed to get out of bed. This day she was cheerful, playing, and seemed entirely well. In the evening, however, she complained of slight earache, from which she had never suffered before, but on Monday, January 11, she was up and about. Toward evening she began to complain that her hip hurt her, and she was hardly able to walk. On Tuesday, January 12, she vomited before she was out of bed. Later in the course of the morning she got up, but in the afternoon vomited several times and went back to bed. She still complained of her hip hurting, and any pressure upon it seemed to make her shake all over. The mother noticed also that there was a jerking, irregular character to her speech. These were the first distinct nervous symptoms, and her mind seemed entirely clear. On the morning of Wednesday, January 13, the child was scarcely able to stand, and the mother now noticed the irregular movements of the eyes and eyelids. On this day she seemed dazed. Dr. McCombs described it as "a state of fear." She could not well be quieted, and in the afternoon her mental state became worse, and in addition she could not sit unsupported. About 9 o'clock in the evening she began to scream violently, sometimes for an hour at a time, almost without pause. This continued until 4 o'clock on the morning of the next day, January 14. She was pale and trembling; half delirious; there was apparently no disturbance of the tactile sensation, and she could feel wherever she was touched. After about two hours' sleep she started to scream again, and was taken during the day to the Children's Hospital, four days after the onset of the acute symptoms.

Examination on admission, January 14, showed a well-nourished child of good color. The mind did not appear entirely clear, but there seemed to be no special excitability. She could utter a few words, but with great difficulty, and the speech was very jerking and irregular. There was a very high degree of lateral nystagmus nearly always present, but growing worse in paroxysms and increased on ocular exertion, and accompanied by a fluttering move-

ment of the eyelids. The patellar reflexes were increased. There was a decided incoördination of the muscular movements of the extremities. A few mucous rales were heard in the lungs; respiration was regular. The heart showed nothing abnormal.

I made an examination of the child for the first time upon the next day, January 15, with the following notes: "The mental condition must certainly have improved, for it now seems nearly normal. She answers questions clearly, but after some delay and with a slight trembling of the voice. There is a curious, very marked fluttering of the eyelids which is not constant; and with this a rapid nystagmus, both lateral and vertical, lasting for a moment and then for a moment disappearing. No paralysis of the ocular movements can be found, and no facial paralysis. The child can whistle and show her teeth when directed. Her grip is good. There is trembling and a very decided ataxia in the movements of the arms and of the hands on attempted effort, apparently not increased by closing her eyes. The patellar reflexes are active, and there is slight ankle-clonus of the right foot, and a suspicion of this in the left foot. The Babinski symptom is absent. She can stand only when supported, and with her feet broadly separated from each other."

On January 16 and 18 Dr. Isaac Jones made careful examinations of the ears to determine whether the nystagmus was otitic in origin. The summary of his report reads as follows: Typical nystagmus and unbalancing of the control of the eye-muscles are present. This is not due to any lesion of the ear, or any disturbance of the vestibular apparatus, because (1) spontaneous nystagmus on looking to the extreme right or left is decreased instead of increased; (2) the hearing is normal; (3) stimulation of the semicircular canals gives the correct normal nystagmus, controlling the oscillations and converting them into rhythmic nystagmus of a vestibular character, with a slow and rapid component. The nystagmus-circuit is, therefore, intact on both sides; indicating normal semicircular canals, eighth nerves, region of Deiters' nucleus, the posterior longitudinal bundle in the pons and its connection with the third and fourth nuclei, and, finally, the third and fourth nerves themselves.

On January 19 an ophthalmological examination was made by Dr. H. M. Langdon and the following report rendered: "Palpebral fissures about equal. In the right eye the pupil measures 4.5 mm.; left eye, pupil slightly smaller. On admission of light the accommodation is normal in each eye. The ocular rotation seems full and equal in all directions, the visual axes being parallel. The eyes are steady on fixation, but on rotation in any direction there develop a few quick nystagmic jerks, usually about five or six oscillations in a group, and then steady fixation will be resumed. The movements were usually accompanied by curious fluttering

of the eyelids. The disks are slightly full, normal in color, with clear margins. There are no changes of the fundus."

Improvement went on with great rapidity. By January 23, nine days after admission, the child could sit up in bed unsupported, with some ataxic movements of the arms on attempting to balance herself. While standing on the floor there were some oscillatory movements of the entire body, but she could now walk if supported by one arm, and her gait was normal, except for a degree of weakness and uncertainty. On closing her eyes she was unsteady, but not to a degree constituting Romberg's symptom. The grip was only fair, but equal on both sides. The patellar reflexes were slightly increased on the left side. No ankle-clonus or Babinski reflex was present. The eyes exhibited a rotary nystagmus as observed before, but to a much less degree. The sensorium was entirely normal; the child answering questions and conversing freely, in contradistinction to the condition earlier in her history, when, although she would answer questions, she made no effort to speak at other times. The tongue was protruded with ease in any direction. No facialis symptom could be elicited. She complained of her feet being constantly cold. She could feed herself fairly well and touch her nose with the eyes closed.

By February 1, seventeen days after admission, it was noted that she still walked with some unsteadiness, but without any support, and with the feet rather wide apart and the body bent somewhat backward in the effort to balance herself. The nystagmus had disappeared except on continued ocular exertion to the extreme of the ocular field. On February 10, one month after the onset of the acute symptoms, she was discharged from the hospital, and the following note was made: "Since admission there has been an entire change of mentality from sluggishness, haziness, and dulness to a condition of alertness and brightness."

The temperature while in the hospital was afebrile, except for a rise to 100° on a single occasion. The Wassermann reaction taken on January 18 was negative and the von Pirquet faintly positive. Lumbar puncture on January 21 gave a dry tap. The urine was examined on a number of occasions, and was practically always negative. On one examination a faint trace of albumin, cylindroids, an occasional hyaline cast, and a few leukocytes were reported. Examination of the blood on the day of admission showed a leukocyte-count of 11,600. The differential count gave polymorphonuclears, 57 per cent.; lymphocytes, 31 per cent.; mononuclears, 7.5 per cent.; transitionals, 3 per cent.; eosinophiles, 1.5 per cent; basophiles, 0.

Treatment consisted on admission in the administration of a purgative and of sodium bromide. After this, on the ground that the condition might be toxic, bicarbonate of soda was given every four hours and enteroclysis every six hours. This treatment was continued until recovery was well advanced.

The noteworthy features in this case consist in the rapid development of symptoms without discoverable cause, unless possibly the child had suffered from influenza; the very uncommon degree of nystagmus; the ataxia of the extremities; disturbance of sensorium; affection of speech; slight increase of reflexes, and the rapid recovery, complete in one month from the onset.

We have here symptoms which, on the whole, point chiefly to some disorder of the cerebellum. That this was the only portion of the brain affected would seem questionable. As Batten[1] has pointed out in an able paper upon "Ataxia in Childhood," it is impossible to draw a sharp line between the cerebellar and the cerebral cases. In some the symptoms pointing to cerebral involvement predominate, and in others, as in the case reported, the cerebellar symptoms are in the ascendency.

In the case I have described, such systemic disorders as Friedreich's ataxia and the cerebellar ataxia of Marie were naturally out of the question. Tumor and abscess of the cerebellum, at first thought to be possibilities, were excluded by the course of the disease and by the examination of the eye-grounds; and that the nystagmus was not otitic in origin was shown by the application of Bárány's tests, although this was not certain proof that the symptom depended upon a cerebellar lesion.

Fickler[2] gives a convenient classification of the diseases of the cerebellum, which may profitably be considered in the effort to place the case described. The first group is that of congenital cerebellar ataxia, from which this case is naturally excluded by the age. The second consists of the acquired cases, which are subdivided into the chronic progressive and the acute forms. The latter, to which this patient naturally belongs, is again divided into (*a*) traumatic (*b*) encephalitic, and (*c*) toxic. According to this classification the encephalitic cases follow especially the infectious diseases. The toxic cases would be represented in early life by those depending upon gastro-intestinal auto-intoxication. The anatomical difference would appear to be that in encephalitis there is an actual inflammatory process active, and in the toxic cases the condition in the acute stage is one of cellular degeneration. Clinically it would seem difficult to make a sharp distinction, and the two may be conveniently grouped in this connection under the heading of acute non-suppurative encephalitis, or acute hemorrhagic encephalitis.

The acute infectious diseases are the most frequent of the causes mentioned. In epidemics of poliomyelitis, too, cases are not infrequently seen with the symptoms of encephalitis, alone or in combination with spinal symptoms. The process in this disease is known to be an inflammatory one; and yet the recovery may be

[1] Brain, 1905, xxviii, 484.
[2] Deutsch. Zeitschr. f. Nervenheilk., 1911, xli, 306.

so complete in some instances that, in the absence of any other satisfactory explanation, the case recorded here might perhaps be assigned to this group; in this instance, most unusually, the cerebellum bearing the brunt of the attack. Against this supposition, yet not completely excluding poliomyelitis as the etiological factor, is the fact that nearly always the lesions in this condition are more widely disseminated than in the present case.

In the large majority of cases of uncombined acute hemorrhagic encephalitis the process is limited to the motor region of the cerebrum. In many it is seen also in, and in a very few cases it is confined entirely to, the region of the pons and medulla. In other cases, much less numerous than the first class, the encephalitis, as stated, attacks especially the cerebellum. In this event there is the comparatively sudden development of the symptoms of encephalitis in general, such as fever, unconsciousness, convulsions, and the like, lasting a variable time, although in the end the cerebellar symptoms predominate. The most characteristic of these are ataxia, staggering gait, and vertigo; although often associated, but not certainly cerebellar in origin, are nystagmus, disturbances of speech, and tremor.

The prognosis of the great majority of cases of acute non-suppurative encephalitis, whatever the location, is favorable as far as life is concerned, and favorable, too, as regards improvement; but less so as regards complete recovery of power and of a normal mental condition.

Batten details several cases similar in many respects to the one I have reported, and publishes others collected from medical literature; and there are still a number of others not found in his series. I append abstracts of all the cases I have been able to discover. Only those are included in which the course of the disorder was sooner or later arrested and improvement followed. Those showing a progressive increase in the symptoms do not belong to this category.

(1) Shepherd (*Med. Times and Gazette*, 1868, i, 144). Girl, aged five years. On the second day of scarlet fever she became speechless. Examination a month later showed her unable to speak, write, or stand; her head and arms fell forward; her legs were weak. After three weeks she improved rapidly and could walk, although with an ataxic gait. Gradually she became more intelligent. In about three and one-half months from the onset she could play about the ward, although her movements and speech were far from normal.

(2) Schepers (*Berl. klin. Wchnschr.*, 1872, ix, 517). Girl, aged eight years. On the fourth day of measles she became unconscious, and later exhibited aphasia and then marked ataxia of the limbs. The intelligence seemed unaffected; the sensibility normal. In one and one-half months she began to speak, but with an altered

voice; she could stand supported, but not walk; there was great ataxia in the hands. A week later she walked with an ataxic gait. Memory had been largely lost, but she learned rapidly, and several months later rejoined her original class in school. Schepers speaks of the favorable outcome, but does not state whether any traces of the disorder remained.

(3) Feith (*Allg. Zeitschr. f. Psychiat.*, 1873–4, xxx, 236). Boy, aged five years. Typhoid fever was followed by aphasia, ataxia, and unconsciousness. After three weeks improvement took place in the mental state, but he still could not stand. Later he had psychic disturbances and a distinctly ataxic gait, and this condition lasted three weeks. About two months after the onset he seemed to have recovered completely. No reference is made to any ataxia of the upper extremities.

(4) This case is the only one in the series following trauma. The question could be raised whether it should properly be included here, inasmuch as the ataxia was of slower development than in the other instances. It seems to me, however, rapid enough to be called acute:—

Bastian (*Lancet*, 1878, ii, 207). Girl, aged ten years. She fell down stairs striking the occiput; experienced no loss of consciousness, but suffered from pain in the head on the next day. Two weeks later she had another fall on the occiput. After this she grew worse, and in two weeks was having vomiting and occipital pain. She was sent to the hospital eight weeks after the first fall. One week later, when attempting to get out of bed, she was found to stagger badly. Soon after this the sight became impaired. When seen again six months after the first accident she had a drunken gait; incoördination of the hands; optic neuritis; pain in the head; normal intelligence. She grew worse for a time, but after about three months improvement began, and in two months more she had perfect power in the upper extremities. By about a year after the fall she was entirely well, except a slight affection of gait.

(5) Lenhartz (*Berl. klin. Wchnschr.*, 1883, xx, 312). Boy, aged eight years. Acute dysentery was followed promptly by a brief maniacal state, and then entire loss of speech; anesthesia; paralysis of the sphincters, and mental weakness. Two weeks later he had nystagmus and marked ataxia of the head, extremities, and trunk. The aphasia and ataxia lasted for months, and he could not speak for three months. At the end of two and a half years there was only a little ataxia and slowness of speech and a deficiency in intelligence.

(6) Hammarberg (*Nord. med. Arkiv.*, 1890, xxii, No. 23). Male, aged seven years when he had pertussis, and soon after this "inflammation of the brain," with unconsciousness for a short time. This was followed by rhythmic swinging movements of the head; incoordination of the arms; loss of speech; inability to walk, and mental

disturbance for a short time. The condition remained unchanged for three months and then gradually improved. About one year after the onset the ataxia had lessened and he could walk unaided, but the gait was uncertain and reeling. The patient finally returned to school, but his gait continued to be always uncertain; the speech scanning and slow; he could not write well, and his disposition was altered for the worse. At the age of twenty-two years he had inflammation of the lungs, and after this gradually became insane and died at the age of twenty-four years.

(7–9) Lüthje (*Deutsch. Zeitschr. f. Nervenheilk.*, 1902, xxii, 280). Three cases occurring in one family, all developing during severe typhoid fever.

(7) Boy, aged ten years. Unconsciousness developed on the fifth day of the fever. This persisted for seven weeks, and afterward he remained dazed for over a month more and could not speak. During this time there were rhythmic movements of the head. When discharged from the hospital, four months after the onset, he could walk only with support; had ataxic movements of the legs and of the left arm; disturbance of speech, and ataxic nystagmus.

(8) Girl, aged seven years. Had unconsciousness for weeks, with oscillatory movements of the head, grinding of the teeth, and twitching of the face. She gradually improved and then showed decided ataxic movements of the extremities. Two and one-half months after the onset there were still imperfect speech; marked ataxia of extremities; unsteady gait; active tendon reflexes, and ankle-clonus. The sensibility was not affected, and there was no nystagmus or psychic disturbance. Three weeks later the gait and speech were still affected, but the upper extremities were normal.

(9) Boy, aged six years. He had a dazed condition for one and one-half months, and did not speak for two weeks more. Meantime there were rhythmic movements of the head, and marked ataxia of the trunk and extremities. No effort to speak was made until after one and one-half months, and then the speech was slow and scanning. He improved rapidly, and about two months from the onset he had remaining only a slight disturbance of speech and of gait.

Lüthje summarizes the principal symptoms of all three cases as follows: Severe typhoid fever followed by unconsciousness lasting for weeks; gradual recovery of mentality; severe ataxia in all the muscle groups, without paralysis or disturbance of sensation; slight disturbance of intelligence affecting the memory; scanning speech and increased reflexes.

(10) Taylor (*Lancet*, 1904, ii, 1416). Boy, aged four years. Six weeks before he was admitted to the hospital he had a slight fall, but without striking the head; three weeks later he had pertussis; four days before admission he developed twitching of eyes,

hands, and feet, and was unable to walk. Examination showed trembling of the limbs and the trunk, suggesting disseminated sclerosis; inability to speak plainly or to walk alone; nystagmus. In twenty-two months he could walk with a drunken gait when supported; the arms were ataxic; the speech hesitating; the mental condition good. By three and one-half years after the onset he was reported to be nearly well, although the speech was still a little imperfect. Examination over twenty years later showed the recovery complete.

(11) Voelcker (*Brain*, 1905, xxviii, 360). Girl, aged four and a half years. Scarlet fever was followed by unconsciousness lasting two weeks; no vomiting. Then the speech was found to be lost and she could not feed herself. Improvement gradually followed and when examined three months later she could not stand; the gait was ataxic when supported; there was some ataxia of the upper extremities; tremor of the head; brisk knee-jerks; variable plantar reflexes; no ankle-clonus; slow and indistinct speech. Two months later (five months after the onset) she showed little improvement; the knee-jerks were less active; the ataxia less; the mental condition improving. One and a half months after this the symptoms were still very marked.

(12) Guthrie (*Brain*, 1905, xxviii, 363). Girl, aged seven years. During measles there occurred vomiting, convulsions, squint, and unconsciousness. After five days she was better, but could not speak. Aphasia persisted, and there developed exaggerated knee-jerks; incoördination of upper and lower extremities; anesthesia and loss of sphincter-control. She improved gradually, and in three months could stand, talk, and feed herself. Sixteen months after the onset there were drawling speech; slight ataxia; tremor of the upper extremities; ataxic gait; brisk knee-jerks; ankle-clonus at times. She was mentally slow.

(13) Batten. First case. (*Brain*, 1905, xxviii, 489.) Girl, aged four and a half years. Immediately after influenza she developed vomiting, and in a week paresis of the legs and affection of speeeh; slight involvement of the sphincters; no loss of consciousness and never headache. A month and a half later she showed a wildly ataxic gait when supported, and could barely stand alone. There were marked incoördination of the hands; somewhat bulbar articulation; slight paresis of the left side of the face; active knee-jerks; doubtful ankle-clonus. There was no nystagmus. Examination three months after this showed that recovery was complete.

(14) Batten. Second case. (*Ibid*,, 490). Boy, aged three and a half years. Measles was followed by convulsions and unconsciousness lasting a week. Two months later there were slow speech; marked ataxia of the arms and legs; slight ankle-clonus, and perverted moral sense. There was no nystagmus. After one and a half years he was very much better. When seen last, April, 1907

(*Clin. Soc. Trans.*, 1907, xi, 276), there was still slight incoördination of the legs, although the gait was good; the speech was rather slow and hesitating, and the mental condition rather backward for the age.

(15) Batten. Third case. (*Clin. Soc. Trans.*, 1907, xi, 276). Boy, aged eleven years. Without known cause he developed headache and on the next day falling; inability to feed himself, and vomiting. On the sixth day he had a drunken gait; ataxia of both legs, but less in the hands; nystagmus; active knee-jerks; loss of tone in the limbs; no affection of sensation. He improved rapidly and in a little over three weeks showed only slight ataxia of the lower extremities.

(16) Batten. Fourth case. (*Ibid.*, 277). Boy, aged twelve years. He had had petit mal for some years. After a severe attack he suffered from unconsciousness for three days. Following this there were no control over the arms or legs; slow and jerking speech; unsteadiness of the trunk and head; poor mental condition; intention-tremor; no vomiting or headache. He had not been able to walk for over six months, and when aided had a wildly ataxic gait. The knee-jerks were active. He improved but little while under observation.

(17) Nonne (*Neurolog. Centralbl.*, 1909, xxviii, 885). Boy, aged twelve years. During an epidemic of poliomyelitis he developed an encephalitis with cerebral symptoms, especially Jacksonian epilepsy, and subsequent hemiplegia. He was unconscious for a week. After subsidance of the cerebral symptoms, he showed general disturbance of coördination, affecting even speech and the muscles of respiration. In the course of two months the symptoms subsided, and in three months he was completely well.

Among more than doubtful cases not included in this series may be mentioned the following:

Marie and Joltrain (*Rev. Neurolog.*, 1910, xx, 123). Boy, aged fourteen years. He had typhoid fever at five years, followed by difficulty in speech, in walking, and in some of the movements of the extremities. The condition steadily grew worse. There was marked ataxia with complete abolition of reflexes. The mental state was normal.

This case, although beginning apparently acutely, had shown such a progressive increase of symptoms that it is rather to be placed in the category of "chronic progressive ataxia."

Baudoin and Français (*Rev. Neurolog.*, 1910, xx, 139). Girl, aged seven and a half years. Epileptiform seizures began at three months and continued with irregular and increasing frequency. When examined by the writers at seven and a half years of age the intelligence was little developed; she could express herself very imperfectly; there were slight increase of the knee-jerks on the left side; some hesitation and trembling in the upper and lower extremities, and a cerebellar gait. There was no nystagmus.

The doubt in this case is principally as to the acuteness of the origin, which may, in fact, have been congenital.

Williamson (*Proc. Royal Soc. of Med.*, 1912–13, Section on Diseases of Children, 41). Boy, aged ten years. Tremor began three and a half years before, and the child lost strength and grew less bright. Examination when brought to the hospital showed tremor in the arms and tongue; ataxic gait; brisk knee-jerks; no nystagmus. Seven months later there had been no marked progression of symptoms. A doubtful slight lateral nystagmus was present.

Williamson says that juvenile paralysis could be thought of in the diagnosis. There is nothing in his history indicating an acute onset, and the case hardly belongs here.

The following analysis and conclusions may be formulated based upon the 18 cases, including my own. They are necessarily incomplete, owing to the absence of sufficiently full details in some instances.

The immediate apparent causes of the attacks in the cases as reported are divided into scarlet fever, 2 cases; measles, 3; typhoid fever, 4; pertussis, 2; influenza, 1; poliomyelitis (?), 1; epileptiform convulsions, 1; trauma, 1; dysentery, 1; not discovered, 2. Possibly my own case, placed in the last class, could with reason be assigned to influenza. The preponderance of acute infectious diseases is very evident. Only 1 case followed trauma. It does not appear that the pertussis reported in 2 instances was of sufficient severity at the time to put these cases in the class of traumatism from violence of coughing; but possibly the case following epileptiform convulsions could be placed here. The instance of an attack following dysentery might possibly be an example of ataxia of toxic origin, but the duration was almost too long to permit of this conclusion. Ten of the patients were boys and 8 girls. The age at the time of onset ranged from three and a half years to twelve years, 10 of the patients being six or more years of age.

That the condition present is in fact dependent upon a lesion of the cerebellum is, in a way, an assumption. Only in the patient seen by Hammarberg did the case come to autopsy, and here very serious alterations of the cerebellum were found. This, however, was years after the first appearance of symptoms, the patient meanwhile having become insane and developing new somatic disturbances; and to how great a degree the early acute manifestations depended upon the lesions found must remain uncertain. The complex of symptoms based upon the composite of all the cases seems sufficient, however, to warrant a belief in the cerebellar origin. That the malady is not dependent upon vestibular or labyrinthine disease was shown in the case now reported by the application of Bárány's tests, and in none of the patients was any impairment of hearing noted. Vertigo, so characteristic a cerebellar or labyrinthine symptom, is not referred to in any of the reports.

The early age of most of the patients makes the identification of this symptom a matter of difficulty.

Disturbances of the sensorium were present in the early states of a large number of cases. Unconsciousness is mentioned in 11 instances, sometimes of brief duration, sometimes lasting for weeks. Convulsions were occasionally seen; delirium was also observed. All these may be classed among the symptoms common to any severe intracranial lesion, or they might be the evidence of a complicating disturbance in other regions than the cerebellum. Some affection of mentality, apart from unconsciousness, was present in 12 instances. In most of these it was of brief duration, but in a few it persisted in some form for a longer time. In such it, of course, indicated lesions elsewhere than in the cerebellum alone. Regarding the disturbance of speech, it is interesting to observe that in 8 cases the patient was for a time entirely unable to speak, and in some instances this condition lasted for months. Later, after the power to speak had been regained, in all but 3 of the cases some affection of it remained for a variable time, and in many was still present when the patient was last seen. It is described as "slow," "drawling," "scanning," "jerking," or "irregular." The affection of speech might with propriety be considered an extracerebellar disturbance, but certainly in some cases at least, and perhaps in most of them, seems not so much to depend upon an involvement of the centres for speech as upon an inability to articulate properly—an ataxic condition. It is possible that in producing the speech-disturbance the medulla may also be involved, and the same is true of the vomiting, which was seen early in some of the cases.

The tendon reflexes were found "brisk" or "increased" in 9 instances. In the others nothing is said upon the subject. Ankle-clonus was present in 4 cases. It is evident, then, that there is a distinct tendency to increase of the reflexes in this disorder, pointing toward the cerebellar involvement. In a few cases "weakness" or "hypotonia" of the limbs is mentioned, but in others it is distinctly stated that no weakness or paralysis was discoverable. In general it is a fair conclusion that the inability to walk or to use the arms depended upon the ataxia rather than upon paresis. The ataxia was noted in every instance; in the legs in all, in the arms it appears to have been present in all but one case. Not infrequently the trunk and the head shared in the incoördination. Anesthesia is mentioned in 2 instances, and more or less loss of control of the sphincters in 3. These symptoms are, of course, not cerebellar. It is to be observed that nystagmus is recorded in but 5 cases; apparently in none of the others as marked as in my own patient. Although it is probable that there exists a cerebellar nystagmus, the symptom is certainly produced by lesions of other regions as well; and this series shows how frequently

there may be a cerebellar ataxia without nystagmus. Optic neuritis was seen in but one instance.

That the lesion is one capable of partial or even complete removal or compensation is shown by the history of the majority of the cases. In 7 it is stated that entire recovery ensued, and it is probable that Scheper's case is to be included here, although the text is not quite clear. In my own patient recovery was complete in one month from the onset of the attack; in Feith's case in two months; in Nonne's case in three months; in Batten's first case the patient was found well in four and a half months. The case of Taylor is of special value from a prognostic point of view. After three and a half years following the onset there were still slight evidences of the disease present, but when seen over twenty years later recovery was complete. In a number of the cases reported the time which had elapsed during which the patient was under observation had been short, and the improvement had been rapid; and it is a fair presumption that many of these recovered completely. There is, indeed, every reason to believe that in most instances few if any evidences of the disease will remain. That, however, severe symptoms may persist a long time and probably always is shown by at least 8 of the cases, and in some of these unfortunately some intellectual or psychic abnormality remained.

PNEUMOTYPHOID, WITH REPORT OF A CASE.

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Pneumonia during the second and third week of typhoid fever is not a rare event. It then expresses itself in various forms, sometimes frank and outspoken, sometimes obscure. There may be a leukocytosis, more hurried respirations, a higher pulse rate, and evidences of a more toxic condition. The sputa may be swallowed, or may be evident and present the usual characteristics of a pneumonia. The pneumococcus may be found in smears of the sputa, occasionally the typhoid bacillus, and very commonly various strains of the streptococci and indifferent bacteria. In other words, the pneumonia may be that due to the pneumococcus or to many other types of organisms, and often is the so-called septic type.

Pneumonia which expresses itself in the first days of typhoid fever is rare. But few cases can be found mentioned in the literature. MacCrae mentions 3[1] as occurring in the patients treated

[1] Osler's Modern Medicine.

for typhoid fever at Johns Hopkins Hospital. One of these developed gangrene of the lung, and typhoid bacilli were found in the sputa. F. Glaser mentioned[2] a patient who had consolidation of the lower lobe in the early days of typhoid. This patient had bloody sputa, but no typhoid bacilli were found. An empyema resulted, and in the pus from the pleural sac the bacillus of Eberth was recovered. A. Fränkel[3] makes a statement that the primary localization of typhoid bacillus in a lung with the production of pneumonia is clinically unknown.

The subject of this report is of exceptional interest because she presented a frank, outspoken lower-lobe pneumonia in the first days of what proved to be typhoid fever, and the rare occurrence of the clinical type makes it worthy of a report.

The patient was Mrs. S. T., married, born in Greece, aged twenty-three years, was admitted to the Presbyterian Hospital, Chicago, on November 29, 1913. She was unable to speak English, but through an interpreter it was learned she had been ill for about one week. The illness began with a mild chill followed by fever. Chilliness with high fever continued until she was admitted to the hospital. From the beginning of the illness there was moderate pain in the right lower chest. There was moderate cough with a slight expectoration of yellow, tenacious sputa. The patient was weak, without appetite, bowels constipated, and she suffered great thirst. She stated that the illness began suddenly, and until the day of the chill she was able to do her domestic work. She was nursing the younger of two children, born five weeks before the illness began. The patient had been an inmate of the hospital in March, 1912, when she suffered from an acute bronchitis. With this exception she had enjoyed good health since childhood. On admission the patient had the appearance of marked illness—face flushed; eyes bright; respiration rapid; tongue coated with yellowish-brown fur; pharynx dark red; tonsils small, showing crypts containing yellowish plugs; lips and finger nails moderately cyanotic; both mammæ full and firm; chest symmetrical; right chest expansion less than left, most marked in the lower portion; a high degree of dulness on percussion over the lower right lobe with increased tactile fremitus and bronchophony; bronchial breathing and crepitant rales heard over the entire lower lobe; heart area of dulness, rhythm, and tones normal; pulmonic second sound accentuated; abdomen, rounded contour, flaccid walls, no tenderness; liver negative; spleen easily palpated. No skin eruption. No herpes of lips. Temperature by mouth 104.2° F., pulse 96, respiration 32. Blood: hemoglobin, 80 per cent. Dare; white-blood cells, 12,900; polynuclear cells, 76 per cent. Blood-pressure, Tycos, systolic 115, diastolic 80. Urine: dark amber; acid; 1.022;

[2] Deutsch. med. Wchnschr., October 30, 1912.
[3] Ibid., March, 1899.

albumin trace; sugar, 0; casts, 0; red-blood cells, 0. Sputa: small amount, viscid, mucopurulent, few pneumococci and streptococci, and indifferent bacteria.

A high fever, of a continuous type, with full pulse of 90 to 100, respirations of 30 to 40, and extension of consolidation to the middle and upper right lobes were the chief clinical characteristics in the next two weeks. On the second day in the hospital the white-blood cells numbered 8700 and on the eighth day 12,000. The patient had been managed up to this time as an ordinary lobar pneumonia, involving finally the entire right lung. Because of its long continuance and of an increase of dulness to practically complete flattening over the posterior portion of the right lower lobe a paracentesis was done in this area without obtaining fluid. Then a blood culture was made on December 15, the seventeenth day in the hospital, which yielded a pure typhoid growth. On the next day the washed sputa yielded practically a pure typhoid culture. The typhoid strains in both of these cultures gave positive tests for the typhoid bacillus in lactose litmus, litmus milk, plain broth, glucose agar, and from all cultures the active motile bacillus gave a strong positive Widal with a known typhoid-blood serum. The patient's blood serum gave a positive Widal in 1 to 40 dilution with a laboratory culture of the typhoid bacillus. On December 16 a culture made of the stools was negative of typhoid, but many colonies of Bacillus coli were found. During this period the spleen remained palpable. There was no tenderness of the abdomen, no tympanites of consequence, no roseolar eruption, and no diarrhea. The patient's mind remained clear, although she was ill and restless both day and night.

The patient continued very ill—weak, apathetic, much thirst, absent appetite, with continued fever ranging from 102.5 to 104° F. for the first four weeks, then a slightly remittent character ranging from 101 to 102° F. in the mornings to 103 to 104° F. in the evening until March, 1914. From March onward the temperature was frankly remittent and septic in type. The respirations ranged from 30 to 40 in the earlier stages of the disease, then diminished to 20 to 30 until the last two weeks of the patient's life, when the highest record was 36 per minute. The pulse was full, not very rapid, and of good quality for the first four weeks. After January 1 it rapidly increased and the quality became poor; the rhythm was regular. The blood-pressure gradually fell on December 24 to 105 systolic and 70 diastolic; on February 29 it fell to 90 systolic and 60 diastolic, where it remained until the end. The spleen continued palpable. No rose spots of the skin appeared at any time. The urine remained practically free of albumin, and contained only a few hyaline and hyalogranular casts at times. Cultures made from the urine revealed no typhoid bacilli at any time. Cultures of the stools made in the later stages revealed no typhoid bacilli. Additional

cultures of blood and sputa yielded typical growths of typhoid bacilli after three months in the hospital. Anemia gradually supervened, and on March 25 the red-blood cells numbered 3,650,000; hemoglobin, 55 per cent.; white-blood cells, 12,500; with small lymphocytes 7; large lymphocytes, 14; large mononuclears, 3: polynuclears, 76 per cent.

The consolidation of the whole right lung persisted; gradually softening occurred in the anterior upper lobe with all of the characteristic evidences of cavity formation. Moist bubling rales and amphoric breathing were present over the upper lobe. Moist rales and bronchial breathing persisted in the lower right lung. The sputa became more abundant, contained elastic fibers, pus, and blood cells, typhoid bacilli, pneumococci, streptococci, and many indifferent bacteria. Numerous examinations failed to reveal the bacillus tuberculosis. During the last week hypostasis occurred in the left lower lobe. During the whole clinical course the mind remained practically clear. Although forced feeding was practised, emaciation was present. Death from exhaustion occurred on April 25, 1914, a little more than five months from the initial chill. An autopsy could not be obtained.

The patient's treatment in the early stages was that for pneumonia; after two weeks the treatment was that for typhoid fever. At one time 60 to 90 grains of urotropin were administered daily without any noticeable result. Supporting treatment, with strychnin by mouth or hypodermically and digitalis from time to time, was the chief drug therapy.

The notable events of this case history are as follows: The patient was seized suddenly with chill and fever and presented all of the physical phenomena one week later of a frank right lower-lobe pneumonia. A palpable enlarged spleen was found. Inasmuch as we have found an enlarged spleen in many of the Greek patients who are treated in the hospital for illnesses not usually associated with enlarged spleen, and on that account believed to be due to a malaria suffered in Greece, but little importance was placed upon this enlargement of the spleen. The leukocytosis of admission became less, with an increase of the consolidated area of the lung. On the seventeenth day in the hospital there was a positive typhoid-blood culture, and on the next day almost a pure typhoid growth was found in the sputa. The typhoid bacteremia and typhoid bacilli in the sputa persisted for more than three months, and were probably present at the time of death. The typhoid bacillus was not found at any time in the stools or in the urine.

Therefore this patient seems to present an example of typhoid fever presenting its primary manifestations in the lung in the form of a frank, outspoken croupous pneumonia.

MILD DIABETES IN CHILDREN.[1]

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The fatality of diabetes in early life is an axiom that has come down to us through generations of text-books as a hoary tradition.[2] However, an increasing number of observations seems to show that juvenile diabetes need by no means be a mortal disease—that in childhood and youth, as in adult life, diabetes may run a favorable course.

URINE CHART.—CASE I

Date.	Quantity.	Reaction.	Specific gravity.	Albumin.	Sugar. per cent.	Remarks.
Dec. 24, 1910	....	Alkaline	1040	—	Considerable	Diacetic acid, 0.
Dec. 29, 1910	....	Acid	1027	—	Distinct	
Jan. 5, 1911	1500	Acid	1030	—	Distinct	
Jan. 12, 1911	2500	Acid	1025	—	—	
Jan. 14, 1911	2000	....	....	...	Trace	
Jan. 19, 1911	1750	Acid	1018	—	Trace	
Feb. 16, 1911	2375	....	1030	—	Trace	
June 10, 1911	....	Acid	1030	—	Trace	
July 13, 1911	....	Acid	1029	—	—	Oxalates.
Aug. 8, 1911	....	Acid	1019	Faint trace	Trace	
Dec. 11, 1911	2000	Acid +	1028	Trace	0.6	Urates; oxalates.
Dec. 27, 1911	....	Acid	1026	—	0.6	Oxalates.
Jan. 11, 1912	1650	Acid	1030	—	0.55	Oxalates.
May 18, 1912	....	Acid	1020	—	Trace	Diacetic acid, 0.
May 21, 1912	....	Acid	1034	—	Trace by fermentation	Diacetic acid, 0.
Nov. 8, 1913	....	Acid	1010	—	0.5	

Case I.—For several years I have had under observation a boy and a girl—brother and sister—who when they first came to me gave me great concern. The boy, aged nineteen years, had been urged by his father to take out life insurance in order to learn lessons in economy. Though he believed himself perfectly well, he was rejected, naturally to his great consternation, because sugar was found in the urine. Before he came to me another physician had confirmed this fact and had given a gloomy prognosis. The boy had had no sickness of moment, except a mild attack of jaundice four years previously. I placed him on a carbohydrate-free diet,

[1] Read at a meeting of the Association of American Physicians, Washington, D. C., May 12, 1915.

[2] Since reading this paper, the statistics of De Lange and Schippers (Nederlandsch Tijdschrift voor Geneeskunde, 1915, July 24, ii, No. 4, p. 637) have appeared. They found between 500 and 600 cases of diabetes in children recorded; recovery was mentioned in only 30 of the 500 cases, and these were not traced long. They themselves report 8 cases in detail. All terminated fatally, the duration varying from eight or nine months to two years and five months.

but the sugar persisted for a long time. There was usually a trace present at some time during the day, frequently in the morning specimen. The quantity of urine was not increased and there was no thirst. Indeed, aside from loss of weight, probably due to restriction in the food intake, the boy presented nothing abnormal, except a profound mental depression, for which a chance question gave me an explanation. I learned that a medical student had told him that diabetes in the young was absolutely hopeless. The sugar, tested by the reduction and the fermentation method, varied, as is shown in the chart, from traces to 0.6 per cent. Diacetic acid was never present. Without any other than dietetic treatment the boy finally lost his glycosuria, and no longer excretes sugar, though on a normal diet.

Case II.—Shortly after the first case came under my observation, the boy's sister, aged seventeen years, presented herself on account of loss of flesh—in a few months her weight had dropped from 133 to 122½ pounds. She had thirst at times and a poor appetite. Menstruation was painful, but regular. Her color was pale—hemoglobin 70 per cent. The urine contained glucose from a trace to 0.7 per cent. The quantity varied from 1000 to 1500 c.c. in the twenty-

URINE CHART.—CASE II

Date.	Quantity.	Reaction.	Specific gravity.	Albumin.	Sugar, per cent.	Remarks.
Jan. 2, 1911	....	Acid +	1033	–	Trace ?	
Jan. 19, 1911	....	Acid	1040	–	Trace	
Jan. 23, 1911	1500	Acid	1030	–	Trace	
Jan. 30, 1911	1000	....	....	–	Distinct	
Mar. 7, 1911	....	Acid	1025	–	Trace	
Mar. 25, 1911	1250	Acid	1030	–	Trace	
May 27, 1911	1000	Acid +	1032	–	Trace	Diacetic acid, 0.
Oct. 22, 1911	....	Acid	1030	–	0.6	Diacetic acid, 0.
Oct. 29, 1911	....	Acid	1021	–	0.4	Diacetic acid, 0. Acetone, 0.
Feb. 3, 1912	....	Acid	1019	–	0.7	
April 3, 1912	....	Acid	1030	–	0.55	
May 26, 1912	....	Acid	1023	–	0.3	

four hours. (See Chart.) On a strict diet her weight fell to 110½ pounds, a reduction of 22½ pounds from her maximum weight. After ten months the weight began to increase, having reached when the patient was last seen 128¾ pounds. Coincident with this increase there was an improvement in her general condition, the hemoglobin rising to 84 per cent. The sugar has disappeared from the urine. A few months ago she was married and is living in the Middle West, enjoying the best of health.

Case III.—The third patient is E. W., aged twenty-two years, the eldest brother of the two preceding. Aside from an attack of jaundice at thirteen, he had always been well. At any rate, though attending his family for many years, I scarcely knew him professionally until August, 1911, when he came because he was losing weight. Examination of the urine showed a trace of sugar.

He apparently recovered, for I did not see him again until November 6, 1913, when shortly after returning from his wedding trip he began to suffer from attacks of indigestion. His appetite was good, but he refrained from eating on account of the distress that followed. He had noticed that at the height of an attack he would pass a colorless urine. I again found a trace of sugar, although there was no polyuria, no thirst, no real diabetic symptoms. The digestive disturbances yielded promptly to treatment. I have not seen him for eighteen months, but know from his family that he is to all appearances perfectly well.

There is no diabetes in the parents of these patients nor in collateral relatives. A maternal aunt has gall-stones. The other five children (there are eight altogether) are, so far as I know—and at some time or another I have examined every one—free from glycosuria. The parents are exceedingly nervous, and the whole family, except the first patient, are very fond of sweets—so much so that the candy box is never closed.

Case IV.—R. C., a girl, aged fourteen years, born in Russia, has a mother who has been diabetic for nine years. The child was well until three weeks before coming to the Polyclinic Hospital. At that time the mother noticed that she drank more water than usual, and passed urine oftener and in larger amounts, getting up from one to four times a night. She also had a little pruritus vulvæ, mostly on urination. Measles and a possible attack of whooping cough constitute all her previous illnesses. She has been a steady candy eater. Menstruation began at thirteen and has been regular and rather profuse, lasting eight days. The father and the other children—a brother and a sister—appear to be well. Physical examination of the child shows nothing abnormal. She weighs 88 pounds, which is a loss of 7 pounds since the beginning of her illness. The blood examination gave the following results: Red-blood cells, 4,850,000; hemoglobin, 88 per cent.; leukocytes, 12,600; polymorphonuclears, 61 per cent.; lymphocytes, 38 per cent.; eosinophiles, 1 per cent.; color index, 0.91.

In this patient the diabetic taint is more pronounced than in the others (see Chart, Case IV), yet under dietetic restriction she has not only become sugar-free, but has attained a tolerance of 90 grams of carbohydrate.

These four cases, particularly the first three, belong to an apparently well-defined group to which Frank[3] and Salomon[4] have called attention. Among Salomon's thirteen cases, however, only two are under the age of twenty-five. He employs the term diabetes innocens im jugendlichen Alter, although several cases over thirty-five years of age are cited in his list. The salient features of the mild forms of juvenile diabetes are:

[3] Die Therapie der Gegenwart, 1914, lv, 439.
[4] Deut. med. Wchnschr., January 29, 1914, p. 217.

1. The familial tendency—the existence of the disease in several members of the same generation.

2. The quantity of sugar tends to be low; in Salomon's analysis usually under 1 per cent., likewise, except in Case IV, in mine.

3. Salomon found that when 100 grams of glucose were added to the diet, only a small amount was eliminated in the urine, showing a high carbohydrate tolerance. In my fourth case, in which this test was tried, almost no sugar was recovered from the urine.

4. In many cases the blood sugar is about normal; in other words, there is no hyperglycemia.

DIABETIC CHART.—CASE IV

Date.	Quantity urine c.c.	Total calories per diem.	Grams dextrose in urine.	Grams dextrose in diet.	Weight.	Remarks.
Feb. 7, 1915	1200	1450	12	18	84¼	
Feb. 10, 1915	960	1500	11	18	85	
Feb. 11, 1915	900	1500	0	12	85	
Feb. 21, 1915	1475	1350	6	11	86½	
Feb. 25, 1915	1500	1640	3	135	86¼	Oatmeal day.
Feb. 26, 1915	850	380	0	28	86¾	Green day.
Feb. 27, 1915	860	340	0	24	...	Green day.
Feb. 28, 1915	850	240	0	33	86	Green day.
Mar. 1, 1915	1400	340	0	20	...	Green day.
Mar. 2, 1915	900	1640	0	135	...	Oatmeal day.
Mar. 3, 1915	800	1440	0	12	84⅜	
Mar. 17, 1915	1280	1450	0	12	86¼	
Mar. 21, 1915	1500	1700	0	72	88	
Mar. 24, 1915	1250	2000	0	128	89¾	
Second admission:						
April 29, 1915	750	1450	0	8	90¼	
May 1, 1915	1050	1720	0	38		
May 3, 1915	750	2000	0	68	90½	
May 5, 1915	700	1980	Faint trace	94	91½	100 grams dextrose.
May 6, 1915	650	1550	0	12		

The fourth case, the only one in which an estimation was made, showed 0.1 per cent. sugar in the blood on one occasion, and several weeks later 0.149 per cent.

Ketonuria may occur in these patients under a carbohydrate-free diet, but disappears rapidly when starches are given.

The first three of my cases fit very well into the category of so-called renal diabetes. The characteristics of this form, as established by Klemperer, Lépine, Frank, and Salomon, are as follows: The diabetes is mild; the daily output of sugar varies from a trace to 1.5 per cent., and is above this only when the amount of urine is small. The glycosuria is independent of the ordinary carbohydrate intake, and the ingestion of even large amounts of carbohydrate influences the glycosuria only to a slight degree —rarely are more than 20 grams per day excreted. Although the carbohydrate intake affects the sugar output but little within the limits given, it is possible to detect a slight increase under a rich carbohydrate diet and a decrease under a sparse or carbohydrate-free diet. Under a complete carbohydrate withdrawal

the urine may or may nor become sugar free. The fact that in some instances it is impossible to render the patient sugar-free by a withdrawal of carbohydrate is, as Frank points out, not a sign of gravity, but is dependent upon the renal nature of the trouble.

CONCLUSIONS. 1. There exists a mild type of diabetes in childhood and adolescence.

2. The disease is peculiar in its tendency to occur in several members of the same family.

3. The glycosuria is usually moderate, although nervous excitement and other disturbing factors may augment it.

4. Other diabetic symptoms are often slight and may be wanting.

5. The disease is not progressive and may remain stationary or end in apparent recovery.

6. In its general features, it corresponds to the so-called renal diabetes.

FUNCTIONAL RENAL TESTS (PHENOLSULPHONEPHTHALEIN; LACTOSE) IN ORTHOSTATIC ALBUMINURIA.

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OUR knowledge of the subject of orthostatic albuminuria has recently been brought together and presented fully in an excellent article by Ludwig Jehle.[1] Jehle studied carefully, and analyzed, a large number of cases fulfilling the requirements of the condition as usually defined, namely, the excretion of albumin in the urine when the patient is in the erect position and the disappearance of albumin from the urine when the patient assumes the horizontal position. In addition to demonstrating, beyond question, the importance of the lordotic factor in the etiology of orthostatic albuminuria, and confirming the general opinion that the immediate cause is a renal circulatory disturbance resulting in a certain amount stasis, Jehle has also shown, in diuresis experiments, that this disturbance when operative leads to decrease in kidney function with oliguria and a low salt excretion; and, correspondingly, that when the disturbance is eliminated by the resumption of the horizontal posture, there is no impairment of kidney function as measured by the salt and water excretion.

[1] Die Albuminurie, Ergebn. f. inn. Med. u. Kinderheilk., Leipzig, 1913, 808–912.

Jehle's study, while thorough as regards salt and water, did not include the application of two functional renal tests upon which a good deal of reliance is now placed, namely, the phenolsulphonephthalein test and the lactose test. We have had the opportunity to observe 6 cases of orthostatic albuminuria (4 of them patients in the private ward, and 2 in the public wards of the Johns Hopkins Hospital, 1 of the former cases is included, due to the kindness of Professor T. C. Janeway, to whose service the patient was admitted) in which the phenolsulphonephthalein test of Rowntree and Geraghty has been applied, and in one of them the lactose excretion was studied.

The individual cases are of interest in themselves, and may be briefly reported as follows:

CASE I.—H. W., white, male, aged sixteen years. Admitted February 3, 1914.

Complaint. Albuminuria.

Family History. Unimportant.

Personal History. Frequent tonsillitis until he had a tonsillectomy and adenoidectomy six years ago. Typhoid fever two years ago. For a year previous to this he outgrew his strength and was generally run down.

Present Illness. The patient was examined for life insurance one month ago, and albuminuria detected.

Physical Examination. Sparely nourished youth. Slight general glandular enlargement; definite increase in lumbar lordosis; lower pole of the right kidney palpable when the patient stands. Systolic blood-pressure, 125.

Urine. Urine voided while in the horizontal position was negative for albumin or casts, while that voided after standing erect for twenty minutes contained 18 grams of albumin to the liter, but no casts. Urine voided after standing erect for twenty minutes, with one thigh flexed, showed, still, 2 grams of albumin per liter.

Phenolsulphonepthalein excretion (patient recumbent):

First hour	62 per cent.
Second hour	7 "
Total	69 "

Phenolsulphonephthalein excretion (patient standing):

First hour	37 per cent.
Second hour	18 "
Total	55 "

Roentgenogram of Right Kidney after Collargol Injection. Right kidney slightly prolapsed, kinking of the ureter with slight hydronephrosis.

CASE II.—M. M., negro, male, aged sixteen years. Admitted February 4, 1914.

Complaint. Rupture.

Family and Personal History. Unimportant.

Present Illness. Four years ago a bulging appeared in the right groin. This is present when he stands and disappears when he lies down.

Physical Examination. Sparely nourished negro boy. Symmetrical decay of the upper lateral incisor teeth; slight tonsillar and general glandular enlargement; retromanubrial dulness; reducible left inguinal hernia; marked accentuation of the lumbar lordosis. Systolic blood-pressure varied between 118 and 100.

Urine. Numerous observations, with the patient recumbent, showed no albuminuria or cylindruria; while when the patient stood up the urine contained from 3 to 6 grams of albumin per liter and a few finely granular casts.

Phenolsulphonephthalein excretion (patient recumbent):

First hour	64 per cent.
Second hour	11 "
Total	75 "

Lactose Excretion. The test was made in the usual way, by intravenous injection of 20 grams of milk sugar dissolved in 20 c.c. of distilled water, the solution having been previously Pasteurized at 75° to 80° for four hours on each of three successive days. The urine was collected at one to two hourly intervals and tested with Nylander's solution, and by the polariscope, until the reaction for sugar ceased to be positive. Normally, all the lactose is excreted in four to five hours.

The results in this case were as follows:

After one hour	35.6 per cent.
Between one and two hours	40.0 "
Between two and four hours	11.2 "
Between four and six hours	trace
Between six and eight hours	none

CASE III.—W. E. S., white, male, aged sixteen years. Admitted June 16, 1911.

Complaint. "Kidney trouble."

Family History. Negative.

Personal History. Five years ago he had slight indigestion for one year.

Present Illness. The patient was examined four months before admission preparatory to entering West Point Military Academy and was told at that time that his urine was abnormal.

Physical Examination. Practically negative. Unfortunately, no data as to the degree of lumbar lordosis was made in the records. Systolic blood-pressure, 110.

Urine. The urine voided after remaining in bed contained no albumin, but on one occasion a few hyaline and granular casts were found. Two specimens of urine voided after the patient had been erect and walking about contained albumin and a few hyaline casts.

Phenolsulphonephthalein excretion (patient recumbent):

First hour	42.7 per cent.
Second hour	12.9 "
Total	55.6 "

CASE IV.—P. B., white, male, aged twenty-five years. Admitted May 2, 1914.

Complaint. "Stomach trouble."

Family History. Grandfather died of tuberculosis.

Personal History. Practically negative.

Present Illness. Began four years ago with a feeling of general weakness. Eight months ago he noticed dull pain in both legs and paresthesias of the face and scalp. He suffered from an acute gastro-intestinal upset six months ago, and since then has had occasional nausea and abdominal pain after meals.

Physical Examination. A little pallor of the mucous membranes; slight general glandular enlargement and arterial thickening; marked increase in the lordosis of the lumbar spine. Systolic blood-pressure varied between 125 and 120.

Urine. When the patient was recumbent, the urine voided was free from casts or albumin, but urine voided on standing showed, on testing, a definite cloud of albumin but no casts.

Phenolsulphonephthalein excretion (patient recumbent):

First hour	54 per cent.
Second hour	18 "
Total	72 "

CASE V.—T. D. W., white, male, aged twenty-four years. Admitted December 12, 1914.

Complaint. Chronic constipation, albuminuria.

Family History. Unimportant.

Personal History. Scarlet fever in addition to the usual diseases of childhood. Malaria at six. Chronic constipation for six years, initiated by irregularity in going to stool and dependence on cathartics.

Present Illness. Gradual onset one year ago. The patient found himself growing lazy and spiritless. Three months ago his physician discovered a trace of albumin in his urine.

Physical Examination. Practically negative, save for a moderate accentuation of lumbar lordosis.

Urine. While the patient was in bed the urine contained no albumin or casts; when standing erect a trace of albumin appeared

as well as a few hyaline casts. A specimen voided after he had stood for some time in an exaggerated lordotic position contained 2 grams of albumin per liter, but no more casts were found.

Phenolsulphonephthalein excretion (patient recumbent):

First hour	51	per cent.
Second hour	20	"
Total	71	"

CASE VI.—J. A., white, male, aged seventeen years. Admitted to the service of Professor Theodore C. Janeway April 17, 1915.

Complaint. Albumin in the urine.

Family History. Unimportant.

Personal History. He had the usual exanthemata and frequent tonsillitis as a child. An adenoidectomy was done four years ago. Malarial fever during two successive summers, four and five years ago.

Present Illness. On applying for life insurance six months ago, albumin was detected in the urine. Of four subsequent urine examinations, two showed albuminuria, one cylindruria, and two were entirely negative.

Physical Examination. Well-nourished youth. Moderate increase in the lower lumbar lordosis, otherwise practically negative. Systolic blood-pressure, 120.

Urine. The urine voided in the morning after a night in bed was entirely negative for albumin or casts. Exaggeration of the lumbar lordosis, while the patient was in bed, brought out a marked cloud of albumin, but no casts.

On two occasions, after standing in an exaggerated lordotic position for one-half hour to an hour, there was, in spite of a large water-intake, a definite oliguria, and the urine contained 6 grams of albumin to the liter as well as a good many granular casts. After this procedure, although the patient was put back to bed, the urine voided throughout the remainder of the day still contained a trace of albumin, but no more casts were found.

Phenolsulphonephthalein test (patient recumbent):

First hour	46	per cent.
Second hour	18	"
Total	64	"

Phenolsulphonephthalein test (patient standing):

First hour (first fifteen minutes in exaggerated lordosis	52	per cent.
Second hour (up and strolling about)	12	"
Total	64	"

In the above 6 cases the phenolsulphonephthalein test showed that the excretion of this substance was entirely normal, save in two instances. In one, the case of W. E. S., it was 5 per cent. lower than the usually accepted normal. In the other, the case of H. W., it was 14 per cent. lower with the patient standing, than when made in the recumbent position. The latter observation is in accord with Jehle's studies of the salt and water excretion. However, in the case of J. A., is is to be noted that there was no reduction in the amount of the dye recovered in the urine, even when the conditions producing oliguria and the maximum degree of albuminuria were present.

The observation of a larger number of cases will be necessary before definite conclusions can be drawn in regard to this point. Unfortunately, a comparison of the excretion in the recumbent and in the erect posture was not made in the other four patients.

In this connection we may mention the case of a young man sent for study because of supposed renal disease. Our examination of the urine revealed no abnormalities either in the recumbent or in the erect position. The lumbar lordosis was a little exaggerated, however, and on making the patient stand in a purposely exaggerated lordotic position for one-half hour he excreted a trace of albumin and a few hyaline casts. The phenolsulphonephthalein test was made with the patient recumbent, and again in the ordinary erect posture. The amount excreted in the recumbent position was for the first hour, 58 per cent.; for the second hour, 20 per cent.; total, 78 per cent.; while that put out while standing erect was for the first hour, 57 per cent.; for the second hour, 13 per cent.; total, 70 per cent. We do not regard a difference of 8 per cent. of great significance, especially when the readings are high, as in this case.

We should like to call attention, in the instance of H. W., to the fact that a collargol Roentgen-ray plate of the right kidney showed a definite prolapse, with kinking of the ureter, and some hydronephrosis; and we would suggest that, in certain instances, at least, a movable, or a prolapsible, kidney may be a factor in so-called orthostatic albuminuria.

THE EFFECT OF WATER INTAKE ON NITROGEN RETENTION IN NEPHRITIS.

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The notable fact which has been established by study of the metabolism of patients with nephritis, is that there are periods

when organic and inorganic substances are retained in the body to a degree not evident in health. Whether this accumulation be dependent upon an inability of the kidney to excrete these substances, as some believe, or whether these substances are retained in the tissues bound in some abnormal combination, is not at present clear. The net result, however, is the same in that balances between intake and output are either difficult to achieve, or at periods quite impossible. In the nature of the factors operating to effect this retention, we come to one of the fundamental questions in pathological metabolism, concerning which our conceptions are vague and, for the most part, devoid of support. The relation of sodium chloride to edema may be cited as an example. Is the salt retained in the tissues, or is there a failure of the kidney to excrete? Is it the sodium or the chlorin that is the immediate factor, or is the whole question one of water retention with the salt as a passive factor? From facts so equivocal, evidently nothing can be derived that may serve as a principle for rational therapy.

It is, however, evident that even though we are able to achieve the ultimate refinement of accuracy in diagnosis of a renal lesion, treatment must depend very largely on our knowledge of the metabolism which usually accompanies this special clinical picture. Various tests may tell us something of the severity of the lesion, but nothing as to what measures are required to meet the impaired functional ability of the kidney, nor how to facilitate the irreducible minimum of its work.

These studies of the metabolism of patients with nephritis were carried on primarily in the hope of disclosing some facts which might be of help in the treatment of these cases. Years of observation, I must admit, have added only to my feeling of uncertainty and skepticism regarding the procedures commonly used, and in the absence of a single rational principle there seems no guide. It was the plan in this study to take certain definite conditions of diet, etc., as a basis, and to observe effects of alterations of single factors. Since it was desirable to continue observations over considerable periods, the diets often used in metabolism studies could not be employed because the patients too quickly tire of them. For this reason we used the ingredients of an ordinary mixed diet, only preserving some factors, *e. g.*, nitrogen, at a minimum. Complete analyses were made of these diets. At once we meet an obstacle in the comparison of the protein metabolism of a normal man with that of a sick patient. The latter may have difficulty in eating a certain small ration which is quite inadequate for the man in health. Our controls are, on this account, not of so much service as in other studies where the patient is not so sick. They serve simply as a background of the normal response to a definite dietary regimen. As the fuel values of these diets hardly exceeds 1300 calories, it follows that the patient is usually insuffi-

ciently nourished; but it often happens that an adequate amount of food can not be ingested and retained by patients with nephritis at those periods of the disease where these investigations are most instructive. A consideration of the metabolism of undernutrition shows that no source of serious error of interpretation is introduced into the investigation by these conditions. If the food intake be below the immediate requirements of the organism for energy the deficit is made good at the expense of body fat (and stored glycogen). This loss becomes manifested in a fall in body weight. There is even in starvation a marked conservation of protein in the organism, and under conditions of slight undernutrition the protein destruction for energy or heat is extremely slight. Toxic protein destruction is another matter, and need not be considered when the temperature range is normal.

The second feature relative to the diets employed concerns the amount of nitrogen which was purposely reduced to a very low amount. The normal person is constantly tending to a condition of nitrogenous equilibrium between intake and excretion, and if protein food be much reduced there is a gradual fall in nitrogen excretion, until after a few days a balance is struck.

Nitrogen is retained to the body normally under two conditions only: during growth, when muscle tissue is being built up, and during convalescence, after periods of disease that have caused tissue destruction; both conditions demarked by gain in weight. Sharply contrasted with these normal states is the phenomenon peculiar to some types of nephritis wherein for periods of time the nitrogen excreted is considerably less than the intake, and there is, synchronously, a loss in, or stationary, body weight unless edema develops. These generally accepted facts which contrast the nitrogenous metabolism of some types of nephritis with the normal are briefly outlined as a basis for our further consideration.

Methods. The methods of study of metabolism in animals have been adopted, so far as possible, in this work. The ingredients of each diet were weighed before each meal, and particular care was exercised to see that all the food given to a patient was eaten. Like portions of food were taken from the ward pantry for analyses. The preparation of the food was intrusted to a competent nurse who understood and realized her duties. Urine was collected from 6 A.M. to 6 A.M., and at the latter time the patient was required to empty his bladder. The urine specimens were analyzed separately; the feces in periods. Unless specifically noted in the charts the nitrogen of the feces is deducted from the total nitrogen intake for the period.

Nitrogen Retention without Edema. From the study of metabolism in a series of cases of renal disease, it is observed that departures from the normal are noted chiefly in respect to nitrogen or sodium chloride. While with some cases the abnor-

mality affects only nitrogen with others, salt is also retained as well as nitrogen. The remarkable degree of nitrogen retention evidenced in some cases is not generally appreciated, and the pertinent question here arises, What becomes of this retained nitrogen? As an example of one of the questions at issue, the following case is cited when there was a retention of three grams of nitrogen per day.

CASE I.—W. H., aged forty-eight years. Admitted December 17, 1913, complaining of headaches and swelling of the face and ankles.

Excepting pneumonia in 1899, he had had no serious sickness. The present illness began about eighteen months before admission, with dyspnea on exertion. For six months there has been vomiting almost daily, sometimes two or three times a day. There was no gastric distress other than nausea. During this period severe headaches have been frequent, and there have been puffiness of the eyes and swelling of the feet. There have been no visual disturbances. The appetite has been good; bowels regular.

Examination. The patient is poorly nourished, with slight edema of the face. Retinæ hazy, but no exudate or hemorrhages. Moderate cardiac hypertrophy. Systolic retraction in fifth, sixth and seventh spaces outside the nipple; no evidence of valvular disease. Pulse is small and of low tension; blood-pressure, 134 mm. Hg. Liver enlarged, 10 cm. below costal margin in the right midclavicular line; smooth and not pulsating. Slight edema of legs and feet. Blood: hemoglobin, 80 per cent.; leukocytes, 10,000. Wassermann, negative. Urine: 1500 c.c.; specific gravity, 1009; albumin, +; casts, + +; leukocytes, +; phenolsulphonephthalein test, 28 per cent.

The edema subsided quickly and the liver became perceptibly smaller during the first week. The patient was apparently doing very well.

TABLE I.—METABOLIC STUDY OF PATIENT W. H.

Date, December.	Amount urine, c.c.	Nitrogen + albumin, gms.	Nitrogen, gms.	NaCl, gms.	Sulphur, gms.	Phosphorus, gms.	Weight, pounds.
19	1780	5.26	4.34	4.27	0.46	0.56	97½
20	1570	4.19	3.83	3.30	0.41	0.38	96
21	1420	....	3.47	4.12	0.29	0.33	95
22	1550	....	4.14	5.43	0.36	0.30	92½
23	860	3.22	2.98	3.61	0.33	0.27	92
24	1560	5.40	3.95	7.02	0.41	0.34	87½
			22.71	27.75	2.26		
		Ingest	41.75	15.21			
Balance			+19.04	−12.54			

Fluid intake 500 c.c. daily. N : S = 10 : 1

On December 23 there was noted a weakness of the right hand, and the next day the patient showed distinct weakness of all muscles of the right half of the body, including those of the face. There was no change in sensation or of the reflexes. There was no disturbance of consciousness; no headache; no other prominent symptom. The patient felt well, except that he was naturally worried about his paralyses. All of these central symptoms cleared up during the next ten days, so that no residual of the paralyses was detectable.

The marked retention of nitrogen, increased until the climax, was of special interest with this history and in relation with the blood-pressure chart.

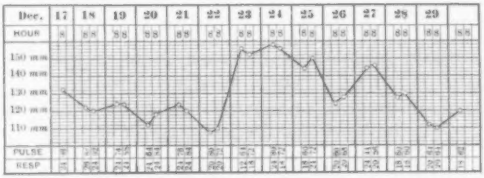

CHART I. Blood-pressure chart. W. H.

Several interesting considerations arise from the metabolic study. The edema which was evident on admission to the hospital subsided rapidly, and explains in part the rapid loss in weight. If this loss were all water it represents nearly five liters, which might seem improbable in view of the moderate edema detectable. There is, however, a difference of over five liters between the fluid ingested and the volume of urine excreted. This fact brings into prominence the lack of concord between the sodium chloride loss and water loss from that necessary for isotonic solutions in the body.

The salient features presented in the study of this case are: a normal water elimination and an apparent washing out of sodium chloride—negative balance—but at the same time marked retention of nitrogen with a climax synchronous with the development of a transient paralysis. The condition of affairs clearly parallels the uremic symptoms which von Leube cautioned are likely to follow the sudden subsidence of edema after diaphoresis. One is led to imagine here a loss of water only, and in consequence of this an increase in concentration of some excretory materials in the blood and tissues.[1] The highest concentration of nitrogen in the

[1] E. E. Butterfield has investigated a series of blood sera, using purely physico-chemical methods. The results are interesting and very significant. The physical changes in the sera of various types of nephritis mirror the more obscure chemical deviations from normal. Thus in the type of case under discussion the slight increase in specific gravity, dry residue, and refraction index means concentration, while the freezing-point indicates a disproportionate increase in some other ingredients.

urine is a little better than 0.2 per cent., and one is led at once to conjecture regarding the total nitrogen elimination had the urine volume been doubled. In other words, is the nitrogen excretion in any degree a function of the urine volume? This case is given, perhaps, unnecessary discussion, since it is in some essential particulars typical of a number that have been studied. It illustrates, as they all do, a relation that appears to obtain quite constantly between marked nitrogen retention and some of the terminal sequelæ of severe nephritis. When there is a rapid accumulation of nitrogen in the body under these circumstances, either uremia, apoplexy, or cardiac failure seems predictable.

It has been accepted that one of the characteristic phenomena of the type of nephritis under discussion is that the nitrogen concentration of the urine is low. While a normal urine may contain 2 or even 3 per cent. of nitrogen, with this form of nephritis the "kidney is not able to concentrate," and a liter of urine may contain even less than ten grams of nitrogen. Concentrations of much below 1 per cent. even when the fluid ingest is restricted are not of unusual occurrence. It would seem, then, from this that the completeness of elimination of excretory nitrogen is dependent upon the amount of diluting medium, other factors being equal; in other words, if the nitrogen to be eliminated is 12 grams, and the maximum concentration effected by the kidney 0.5 per cent., the necessary urine volume must equal 2400 c.c. We have made a number of observations which appear to support this conception.[2] With the following case, which is typical, the evidence recorded in the chart shows that a plus or minus nitrogen balance is dependent on the urine volume, that is, the fluid ingested. In all other respects the periods are exact duplicates.

CASE II.—H. K., aged forty years.

Past History. Patient had scarlet fever at five years of age and pneumonia when twenty-two. Has never been robust, but has been well. No history of nycturia or edema until two months ago. Venereal diseases denied.

Present illness began seven weeks before admission, with headaches, mostly occipital, but involving vertex and frontal regions at times. More recently there has been some shortness of breath, and the patient has grown weaker. At this time there was swelling of the face about the eyes and later some swelling of the ankles. The patient has noted that for the past month he has had thirst at night and passed much urine. There have been cramps in the legs.

This is further emphasized in differences between total dry residue and the protein under various conditions: Normal dry residue minus protein, 1.8; nephritis with edema, dry residue minus protein, 2.2; nephritis with uremia, dry residue minus protein, 3.3.

[2] We have studied 22 cases of nitrogen retention, and these reported represent fair examples.

TABLE II.—METABOLIC STUDY OF PATIENT H. K.

Date, April.	Amount urine, c.c.	NaCl, gms.	Nitrogen, gms.	Weight, pounds.	
9	900	2.88	5.06	119	Metabolic diet.
10	880	2.90	4.85		
11	1920	5.95	9.62		Fluids, 800 c.c.
12	1430	4.72	6.68	117½	
			26.21		
			28.86	(ingest)	
			+2.65	(balance)	
13	2090	6.69	9.64		
14	2190	7.88	11.29	117	Force fluids.
15	1940	6.01	9.31	116½	
16	2220	6.16	9.56		
			39.80		
			29.53	(ingest)	
			−10.27	(balance)	
17	1580	4.27	7.49	114	Milk, 1200 c.c.; water, ++
18	1500	3.45	6.86	113	
19	1840	3.49	8.93	112½	
20	1540	3.23	6.87	111	
21	1760	2.29	8.25	111	
			38.40		
			27.22	(ingest)	
			−11.18	(balance)	
22	1100	1.43	5.47	111	Metabolic diet + fluids, 500 c.c.
23	1030	1.24	5.30		
24	750	2.63	4.50		
25	850	1.02	5.34	111	
26	820	1.48	4.92		
27	910	1.55	5.93	112	
28	1180	2.60	6.68		
			38.14		
			51.10	(ingest)	
			+12.96	(balance)	
29	1300	3.12	7.43	112½	
30	1470	3.09	8.57	....	Force fluids.
May					
1	1480	3.26	6.02	114	
2	1330	2.79	7.75		
3	2290	4.12	11.12	114½	
4	2160	4.01	9.01		
5	2100	4.20	9.60	117	
6	1490	3.13	8.09		
7	1400	2.94	7.84	118	
8	1560	2.72	8.26		
9	1760	2.99	8.55	120	
10	1840	3.50	8.41	119½	
			100.65		
			89.57	(ingest)	
			−11.08	(balance)	

Examination. The patient was a rather poorly nourished man, and looked anemic. The examinations disclosed a moderate degree of cardiac hypertrophy and some edema of the legs. Blood: hemoglobin, 54 per cent., otherwise of no significance. Wassermann reaction negative. Blood-pressure, 178 mm. Hg. systolic. Urine: twenty-four-hour quantity, 1600 c.c.; specific gravity, 1012; albumin, ++; hyaline and granular casts and leukocytes. Phenolsulphonephthalein test; 5 per cent. recovered in two hours. After four days of observation the patient was given the measured diet. An initial diuresis on April 13 was due in part to edema fluid. On the next three days the patient was encouraged to drink water freely. The rise in nitrogen excretion is striking.

In the first period (April 9 to 12) there is a retention of two grams of nitrogen, a minus chloride balance, and a falling weight curve. The loss in weight continues until April 21, when the chloride balance is struck between intake and output. In the second period, April 13 to 16, there is a sharp increase in nitrogen excretion, so that in four days ten grams more nitrogen are excreted than ingested. As the patient began to tire of the diet a change was made to milk from April 17 to 21, involving a slight drop in the nitrogen intake. During this period the patient was urged to take water enough to make the total fluid ingested up to two liters. Here, again, the balance for the period shows a nitrogen loss to the body of eleven grams. The patient's condition had now become excellent, and he was kept in bed only to assure of accuracy in the study.

Thus far the nitrogen excretion has appeared to bear some relation to the volume of the urine. Is this the case actually? If it be so then a restriction of the fluid ingested should be accompanied by a retention of nitrogen in the body, *i. e.*, a plus-nitrogen balance. The fluid ingested was limited to 500 c.c. daily in the period April 22 to 28 and the metabolic diet was resumed. All other conditions were the same as in the earlier periods except that the patient was in much better condition. It is to be observed that the drop in the urine volume consequent upon limited fluid intake is at once followed by a fall in the nitrogen output. On no day did the urinary nitrogen equal the nitrogen of the food, and the period shows a retention of nearly thirteen grams. There was also a rise in the non-protein nitrogen of the blood at the end of the period. There is, then, in this case, an intimate relation between the nitrogen balance and the water excretion.

The increase of fluids in the next period points again to a washing out of retained nitrogen and a negative balance for the period.

One might be inclined to attribute the retention in the period April 22 to 28 to tissue regeneration, because there was a gain of a pound in weight; but this interpretation is negated by the continued gain in the following period, April 29 to May 10, when there was constant nitrogen loss.

A fact in relation to the chloride excretion deserves attention, since it is frequently noted in our studies. From April 9 to 21 the tendency is toward chloride equilibrium, with a more prompt excretion accompanying the periods when the urine volume is large. On April 21 the excretion is the same as the intake. During the next period there is a retention of a slight amount, followed by a negative balance in the final period.

This patient left the hospital in excellent condition and free from symptoms.

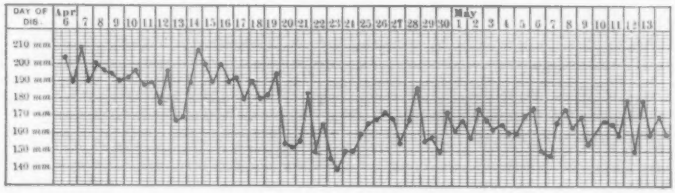

CHART II. Blood-pressure chart. H. K.

The relation between the urine volume and the nitrogen excretion appears with considerable constancy in this type of chronic nephritis. This case given in detail is not exceptional, but rather typical.

The following case presents the same essential factors as the last:

CASE III.—R. B., aged thirty-eight years.

Past History. Patient had scarlet fever in childhood and has had attacks of tonsillitis during his life. Patient was operated upon for appendicitis in 1903. At this time albumin was found in the urine. Has had no symptoms of renal disease until 1914. The patient contracted lues in 1896, and was treated. Several years ago he was treated again with salvarsan.

Present History. For three months there has been increasing dyspnea, especially at night. There has been some cough. He has lost in weight and his appetite is poor. Urine is passed freely, two or three times during the night. There has been very little headache, no visual disturbances, and no notable edema.

Examination. This disclosed slight cardiac hypertrophy, with a blood-pressure of 158 mm. Hg.; no edema; no retinal changes; hemoglobin, 78 per cent.; Wassermann doubtful. The urine amounted to 1075 c.c. for the first day. Specific gravity, 1013; albumin, heavy trace; a few hyaline casts. Phenolsulphonephthalein test, 7 per cent. The non-protein nitrogen of the blood was 88 mg. per cent.

This patient left the hospital much improved, although it was evident that the prognosis was definitely bad. The phenolsulphonephthalein test was never better than 10 per cent. for two hours. In a study conducted on this patient four months later it was found that his kidneys were unable to excrete more than eight grams of

nitrogen per day under any conditions. If the water ingested was adequate to secure a urine volume of 2400 c.c. or over, the nitrogen ran from seven to eight grams, irrespective of how large the protein intake might have been. If, on the other hand, the urine volume were low, the total nitrogen would be low.

TABLE III.—METABOLIC STUDY OF PATIENT R. B.

Date, March.	Amount urine, c.c.	NaCl, gms.	Nitrogen, gms.	Weight, pounds.	
16	1620	6.48	6.77	127	Metabolic diet, + 500 c.c. water.
17	1470	5.29	6.80	....	Non-protein N, 88 mg.
18	1400	4.90	7.66	124	
19	1390	4.45	7.53	123½	
20	800	2.40	4.25	123½	
			32.99		
			36.44	(ingest)	
			+3.45	(balance)	
22	1730	4.00	8.58	124	Increased water intake.
23	1950	3.40	7.56	125	
24	1900	4.20	8.58		
25	1400	3.45	7.54	124½	
26	1840	3.20	7.79	124	
27	1720	3.24	8.43	125	
28	2220	3.45	9.48	125½	
29	1520	1.92	5.16	125	
			63.12		
			50.75	(ingest)	
			−12.37	(balance)	

CASE IV.—D., aged forty years, tailor.

Family History. Father and mother died of old age.

Past History. Malaria in childhood. Has never been sick until the present trouble commenced, six months ago. Alcohol in moderation. Venereal infection denied.

Present Illness. This began six months ago, with headaches in the morning. The headaches were frontal at these times. The patient noted that the breath was foul. The headaches have increased in frequency and the patient has been attending Cornell Dispensary for relief. The eyes have been swollen at times, but not the ankles. He has had frequent urination for two weeks. No dyspnea.

Examination. Well-developed man; looks anemic; face somewhat puffy. Pupils react normally. Albuminuric retinitis on both sides. Thyroid normal. Lungs normal. Vascular: pulse equal, regular, of good force, tension increased; artery, sclerotic. Blood-pressure, 180 mm. Hg., systolic. Heart: precordial impulse heaving and not localized. Relative dulness from right sternal margin to 12 cm. to left in fifth, intercostal space. No murmurs. Aortic

second accented. Abdomen: normal. Liver and spleen: normal. Extremities: no edema; reflexes normal. Glands not enlarged except those in cervical region, which are palpable. Weight: 119.5 pounds. Blood: hemoglobin, 70 per cent. Erythrocytes, 5,000,000. White-blood cells, 18,000. Wassermann negative. Non-protein nitrogen, 132 mg. Urine: 1010 c.c.; specific gravity, 1012; albumin, very heavy precipitate. Many hyaline and granular casts; a few white-blood cells; no red cells. Phenolsulphonephthalein test on March 24, 11 per cent. recovered and a lactose test on the 25th showed no excretion up to fourteen hours. Phthalein test, April 7, 16.7 per cent. in two hours; and on May 5, after discharge, he returned to the hospital for the test, which was 14 per cent. The systolic pressure was irregular from day to day, with limits of 210 and 170 mm. Hg.

As this patient appeared very sick at the time of admission the metabolic diet was not used, but instead milk, in measured amounts, supplemented by arrow-root to increase the caloric value. The metabolic diet was commenced on April 15.

TABLE IV.—METABOLIC STUDY OF PATIENT D.

Date, March.	Amount urine, c.c.	Total nitrogen.	NaCl, gms.	Sulphur, gms.	Phosphorus, gms.	Weight, pounds.	
26	850	7.10	0.51	0.54	0.50	...	Non-protein N, 130
27	1160	10.47	2.90	0.65	0.68	116	mg.
28	1100	8.88	1.65	0.41	0.54		
29	1150	8.70	2.53	0.51	0.54		
30	1490	12.19	3.58	0.67	0.68		
31	1070	7.74	2.14	0.39	0.42	116	
		55.08	13.31	3.17			
	Ingest	45.17	15.66				
		−9.91	+2.35	balance			
April.							
18	2070	7.92	5.38	0.63	0.54	114	Force fluids.
19	2360	9.52	6.37	0.74	0.63		
20	1730	6.64	3.80	0.50	0.46		Non-protein N, 45
21	2910	11.00	8.15	0.82	0.73	116	mg.
		35.08					
	Ingest	29.26					
		−5.82	balance				

NaCl and nitrogen of feces substracted from ingest.

With Case IV there was a negative nitrogen balance attained with relative ease when the protein of the diet was reduced. The flushing out of nitrogen was accompanied by a fall in the non-protein nitrogen of the blood to nearly a normal concentration. The weight remained almost constant. In the second period the fluctuation of the chloride excretion with the urine volume was notable; a phenomenon already mentioned. Chloride metabolism

was not normal, although compensation is attained in an irregular manner; there was no evident edema.

This patient was discharged much improved and sufficiently well to be able to secure life insurance, as he confided to a house officer at the time of a "follow-up" call.

These cases are illustrations of more or less successful application of a principle to attain a definite result: the prevention of nitrogen retention and the washing out of nitrogen retained during some previous period. As a method in practice one must make every reservation as to its efficacy. The cases that are found in hospital wards are, for the most part, representative of advanced stages of the disease where but little benefit at best can be expected. We do not at present know whether periods of nitrogen retention accompany the earlier and often transitory manifestations of renal disease. It is possible only to cite the facts that when this faulty elimination persists for some period and is of a marked degree there ensues some of the phenomena characteristic of uremia. I do not believe we are even able to assert that the latter state is a consequence of retention and not merely an associated phenomenon.

Now it is self-evident that large amounts of fluid can not be taken by every nephritic without danger. Each liter of water ingested represents an appreciable extra burden thrown upon the heart muscle, and with nephritis of all types we find this muscle abnormal and especially so with these cases of nitrogen retention. Hence it follows that with every case caution is necessary, and with some the procedure might be, theoretically, hazardous. A slowly developing water retention has been noted in some cases without evidence of cardiac embarrassment, yet we have held this water retention to be of cardiac origin, and are supported in this belief by the fact that digitalis often causes a prompt elimination of the surplus.

With cases where the renal damage is so extensive that there is no margin of accommodation or where water elimination is impaired no result is secured by forcing of fluids.

The following case is of the latter type:

CASE V.—T. C., aged thirty-eight years.

Past History. Patient has never been confined to bed until the onset of his present illness. He has had slight rheumatic pains at times, but not of such severity as to require medical attention. In habits the patient is moderate; he has used a little beer occasionally, but very seldom whisky. He has had gonorrhea, but never lues so far as he knows, and gives no history suggesting infection. His normal weight is about 110 pounds.

Present Illness. Patient has had headaches for a week; prior to this symptom he believed himself in good health. Three days ago he noted that his face and eyes seemed puffy, but there was

no swelling elsewhere. The urine has been scanty for several days. The color was not noted. He has had no visual disturbances; no dyspnea or nausea.

Examination. Edema of face, especially about eyes. Moderate anemia; pyorrhea alveolaris; cardiac hypertrophy, with a faint diastolic murmur at the left sternal margin and a short systolic murmur at the apex. Pulse not Corrigan type. Lungs seem normal; abdomen normal. Slight pretibial edema; no glandular enlargement. Blood: hemoglobin, 65 per cent.; leukocytes, 6900. Wassermann negative (three tests). Blood-pressure, 160 to 130. Non-protein N, 180 mg. Urine: 800 to 1000 c.c.; specific gravity, 1014; albumin + +; casts and a few erythrocytes. Phenolsulphonephthalein test, 10 per cent. in two hours.

The patient was given the metabolic nephritic diet, beginning April 1. On April 13 this diet was changed to one of milk and arrow-root starch. The patient left the hospital improved so far as concerned symptoms. The headaches ceased and edema subsided. There was no change in the albuminuria. Two weeks after discharge he was readmitted with moderate edema, which disappeared promptly with the use of theocin. There was pronounced diuresis and a fall in weight from 112 pounds to 103 pounds.

TABLE V.—METABOLIC STUDY OF PATIENT T. C.

Date, April.	Amount urine, c.c.	Nitrogen, gms.	N + albumin, gms.	NaCl, gms.	Sulphur, gms.	Phosphorus, gms.	Weight, pounds.	
5	1080	7.08	8.25	4.75	0.44	0.29	110	800 c.c.
6	990	5.89	7.53	3.86	0.35	0.23		water.
7	1040	7.00	8.77	3.95	0.43	0.29		
8	770	4.74	6.54	2.62	0.32	0.15	111	
9	950	7.74	8.61	5.23	0.53	0.39		
10	680	4.46	5.74	2.04	0.34	0.12		
11	840	5.17	6.99	2.52	0.42	0.19	...	2800 c.c.
12	900	5.49	7.08	2.70	0.37	0.22	112	fluid
		47.57	59.51	27.67				
	Ingest	58.12		20.88				
	Balance	+10.55		−6.79			N : S	14 : 1
13	790	4.64	6.12	2.29	0.31	0.17	112	1200 c.c.
14	820	4.77	6.31	2.39	0.32	0.19		milk; 50
15	810	6.60	7.85	2.89	0.43	0.30	113	gms.
16	800	5.18	6.43	2.00	0.29	0.27		starch.
17	850	4.89	6.20	2.72	0.27	0.28	111	
		26.08		12.29				
	Ingest	28.75		10.41				
	Balance	+2.67		−1.88				
							N : S = 16 : 1	

The patient returned to his home but did not attempt to work. Headaches returned in the latter part of May, and there was

dyspnea and some nausea. Edema did not appear. On June 2 the patient's wife noted twitching movements of the hands and face which alarmed her, and hospital aid was requested. The patient had an epileptiform convulsion in the ambulance and was admitted to the ward in coma. Death occurred the day of admission. No autopsy. Clinical diagnosis: chronic nephritis; chronic valvular disease (aortic insufficiency); uremia.

The table in this case shows a low urine volume, with no visible response to increase in fluid ingest; a small negative chloride balance and a marked tendency to retain nitrogen. The high non-protein nitrogen at the beginning of the study indicated that successful therapeutic measures would be marked by a negative nitrogen balance. This could not be secured. In the second period, with even further reduction in the nitrogen ingest, there still persisted a plus balance and the non-protein nitrogen practically unchanged. Here it was evident at the time of the first admission to the hospital that the rapid improvement in the patient's condition could not be continued nor were his kidneys adequate to any larger demands than those of a highly restricted diet. The discussion of cases such as this represents, naturally focusses upon the nitrogen exchange, but the morbid state is hardly more evident with the nitrogen than with other elements concerned in protein metabolism; both sulphur and phosphorus excretion are below what they should be and there are no compensatory days. With these facts in view the terminal event is entirely logical and was expected.

Everyone who has studied the metabolism of cases of nephritis has observed a retention of amounts of nitrogen in excess of what can be explained by increases of the non-protein nitrogen of the blood. A retention of a gram a day is common, two or three grams a day for a couple of weeks not rare. What becomes of fifteen or twenty grams of nitrogen so retained by a patient whose condition excludes the idea of cellular growth? Not half this amount of nitrogen can be accounted for in the blood on the basis of the degrees of the non-protein nitrogen observed.[3] It is evident that the surplus must be in the tissues, either free or combined.

In an attempt to gain some light on this point a series of analyses has been carried out on various tissues from cases of nephritis in comparison with other diseases, and it is apparent that the non-protein nitrogen in tissues accumulates to a remarkable degree. This is true of muscle (psoas) and of liver tissue, whether of all we are not as yet prepared to state. The fact is mentioned in this place as an answer to questions already brought out in this paper.

[3] The normal non-protein nitrogen of the blood reaches its high level at about 40 mg. per 100 c.c.; 200 mg. per 100 c.c. is an exceptionally high figure with severe nephritis. The difference of 160 mg. per 100 c.c. accounts for 4.8 gms. nitrogen if the blood volume equal 3 liters.

Any further consideration of these facts or endeavors to interpret them would be, with the evidence at hand, idle conjecture.

Conclusions. The retention of nitrogen is one of the common phenomena associated with a large percentage of the cases of nephritis observed in hospitals. Whether this retention characterizes also, in lesser degree and periodically, earlier stages of the disease is not at present clear; but this is generally assumed to be true and is held accountable for some symptoms, whether correctly one may not assert. At those periods of nephritis when patients are forced to seek hospital aid the retention of nitrogen outside of convalescence appears to precede and lead up to either frank uremic manifestations or to the graver complications of renal disease. Furthermore, a careful study of a large number of cases discloses many where the metabolic disturbances seems confined to the protein economy, that is to say, the notable failure in elimination is in respect to nitrogen and this retained nitrogen is found not only in the blood but also in the tissues.

With some of these cases water metabolism is either normal or approximately normal and the total nitrogen elimination then appears to depend directly on the volume of water that passes through the kidneys. This is simply another way of stating an accepted fact: that the diseased kidney can not excrete a concentrated urine, *i. e.*, the power of concentration is impaired. If under these conditions the nitrogen of the diet be reduced to about half the normal and the fluid ingested be increased there results first a sweeping out of retained nitrogen and later normal approximations toward equilibrium. Reduction of nitrogen intake alone does not suffice, nor does the ingestion of large amounts of water if the diet nitrogen be not curtailed.

From a practical point of view this principle would seem to have a therapeutic application, although perhaps of narrow scope.

THE DIFFERENTIATION OF NEPHROPATHIES, CARDIOPATHIES, AND ALLIED CONDITIONS.

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The diagnosis of renal insufficiency at present rests chiefly on the establishment of a diminished rate of elimination of certain substances normal or foreign to the usual body metabolism. It is

improbable that any single, simple test will ever completely supplant a quantitative study of the water, chloride, and nitrogen balance, especially when this is supplemented by a quantitative test of the rate of elimination under conditions of stress, *e. g.*, 10 grams of sodium chloride, 3 liters of water, or 20 grams of urea added to the diet. To conduct such a metabolism study successfully requires several weeks and necessitates working with a constant or analyzed diet, besides careful separation, collection, preservation, and analysis of the twenty-four-hour urine during the period of study. It imposes, therefore, on the patient, personnel, and analyst conditions which are difficult to realize at present, either in hospital work or in private practice, even in isolated cases, and which are almost excluded as a routine procedure on a large material. It is highly desirable to have some alternative procedure which is more rapid and convenient with as little sacrifice as possible to thoroughness, accuracy, and reliability.

It is well known that the delayed elimination of certain substances in the usual forms of nephritis results eventually in the retention of these substances in the body. At present there is a lack of definite information concerning the quantitative distribution of the retained substances throughout the body fluids and tissues. It is known, however, that an increased concentration of certain substances in the blood serum occurs in many cases of nephritis. Furthermore, the blood serum is the most accessible material to study for evidence of changes in concentration, which would result from retention of sufficient quantities of the substances in question.

Through the work of Widal and his collaborators, of H. Strauss, and of P. v. Monakow, the existence of two definite forms of nephritic retention has been established. In one form water and salt are retained, while in the other there is retention of nitrogenous substances. In some cases both forms of retention occur together. While this information has been derived chiefly from metabolism studies, it would seem logical to suppose that a sufficiently prolonged retention would be followed by characteristic changes in the blood serum. The detection of these changes in the serum would depend largely on a fortunate selection of methods. Chemical methods alone would not always yield the information desired. A determination of the concentration of sodium chloride, for example, would reveal little or nothing if both water and salt were retained in corresponding amounts. Nevertheless, the resulting dilution of the serum with aqueous salt solution could be detected by physical methods. H. Strauss[1] made use of the refractometer for this purpose, and thereby called attention to the hydremic state of the blood serum, as estimated by the low refractive index, in cases of nephritis with edema.

[1] Ztschr. f. klin. Med., 1906, lx, 501.

Other physical methods may be used to detect different changes in nephritic blood serum. The freezing-point, for example, may be taken as a measure of the concentration of relatively simple molecules, irrespective of their chemical nature. Although the freezing-point method has been more or less abandoned of late, previous reliable work has shown that there is an increased depression of the freezing-point of the blood serum in most cases of uremia. Determinations of the specific gravity have also been used to detect changes in the composition of blood serum, and hydremic sera have been recognized previously by this method.

The numerical values of the freezing-point, refractive index, and specific gravity of normal human serum are practically constants. In the pathological sera the freezing-point, refractive index, and specific gravity not only deviate from the normal, but may also vary independently of one another. These independent variations represent changes in the concentration of entirely different groups of substances. Consequently, the systematic use of these methods would seem especially applicable to the problem of nephritic retention, and should yield valuable results in the diagnosis of cardiopathies and nephropathies. This is in fact the case, and it has been possible with these methods to establish characteristic serum pictures for (1) chronic nephritis with edema, (2) chronic nephritis with uremia, and (3) chronic nephritis with both edema and uremia. Furthermore, chronic nephritis with edema may be differentiated from cardiac decompensation with edema by analysis of the serum. Finally, it is possible to recognize a group of cases which cannot be classified either as primary cardiopathy or nephropathy. These cases show persistent hypertension and an extremely concentrated serum.[2] In the absence of more detailed knowledge they may be designated provisionally as cases of primary arteriosclerotic hypertension.

In the present study the determination of the freezing-point, refractive index, and specific gravity have been supplemented by determination of the protein content and dry residue of the serum. While these supplementary determinations do not add materially to the results, they furnish a striking demonstration of the relatively large variations which are possible in the solid constituents of the blood serum in different diseases.

METHODS. The *freezing-point* was determined with the Beckmann apparatus. The customary precautions as to supercooling and inoculation were always observed. The determinations were made in duplicate, often in triplicate, and are accurate to 0.002° C. The freezing-point is designated as F. P. The freezing-point of blood serum is always below 0° C., and the numerical values are consequently minus quantities. An increased freezing-point in the text refers to one farther below zero, or with a greater absolute value, than that of normal serum.

[2] W. H. Veil, Deutsch. Arch. f. klin. Med., 1913, cxii, 504; and 1914, cxiii, 226.

The *refractive index* was determined with the Zeiss immersion refractometer. The expression $\triangle N_d \times 10^3$ represents the difference between the refractive indices of serum and water at the same temperature multiplied by 1000. This makes the numerical results more striking to the eye without affecting their validity in any way.

The *specific gravity* was determined with an Ostwald pycnometer. The figures given are corrected for temperature and bouyancy of air. The specific gravity is designated as sp. gr. in the tables.

Group.	Case.	Freezing-point.	Δ Na $\times 10^3$	Specific gravity.	Dry residue.	Protein content.
I. Normals:	1 F	0.55	16.8	1.027	9.5	7.9
	2 B	0.56	17.0	1.026	....	7.7
	3 R	0.59	17.8	1.026	9.9	8.5
	4 E	0.57	17.9	1.027	....	...
	5 F	0.57	18.0	1.027	10.0	8.2
II. Cardiac Decompensation with Edema:	1 H	0.55	19.2	1.030	10.8	9.2
	2 L	0.58	17.3	1.026	9.7	8.0
	3 C	0.56	17.0	1.025	9.5	7.8
	4 H	0.56	16.4	1.024	9.1	7.4
	5 Z	0.53	16.0	1.024	9.1	7.4
	6 H	0.54	16.0	1.024	9.0	7.5
III. Chronic Nephritis with Edema:	1 H	0.59	11.0	1.015	6.3	4.3
	2 H	0.53	11.3	1.016	6.6	5.0
	3 F	0.53	11.5	1.016	6.9	5.1
	4 T	0.55	12.6	1.017	7.1	5.6
	5 K	0.57	12.8	1.020	7.2	6.1
	6 F	0.56	12.8	1.021	....	5.7
	7 D	0.54	12.9	1.020	7.3	...
	8 R	0.55	12.9	1.020	7.2	5.6
	9 G	0.56	13.0	1.019	7.6	5.7
	10 V	0.59	13.2	1.017	7.5	...
	11 P	0.56	13.5	1.019	8.8	5.7
	12 R	0.54	13.5	1.018	7.7	6.0
	13 M	0.55	14.2	1.021	8.0	6.2
	14 R	0.55	14.2	1.022	8.4	6.6
	15 G	0.56	14.3	1.023	8.0	6.3
	16 T	0.55	14.5	1.023	8.1	6.7
Sept. 28	17 G	0.57	13.1	1.022	7.3	5.8
Oct. 7	17 G	0.55	14.3	1.022	8.1	6.6
July 27	18 K	0.55	13.8	1.020	8.1	6.3
Oct. 7	18 K	0.56	14.8	1.022	....	6.7
IV. Chronic Nephritis with Uremia:	1 V	0.76	18.9	1.030	10.8	8.3
	2 P	0.68	18.9	1.030	10.7	8.4
	3 C	0.67	18.3	1.027	....	...
	4 L	0.66	18.2	1.030	11.4	9.0
	5 K	0.62	17.1	1.028	....	...
	60'S	0.61	16.5	1.027	11.1	7.8
V. Chronic Nephritis with Edema and Uremia:	1 G	0.61	15.4	1.025	8.5	7.8
	2 P	0.63	14.4	1.022	8.2	5.9
	3 C	0.62	13.3	1.022	7.4	5.3
VI. Arteriosclerosis with Hypertension:	1 G	0.59	20.8	1.033	12.2	9.8
	2 H	0.56	20.7	1.031	11.4	9.4
	3 W	0.56	19.7	1.030	11.6	9.3

The *protein content* was determined gravimetrically after precipitation by alcohol. The *dry residue* was determined in the customary manner. The results of the determinations of the protein content and dry residue are expressed as percentage weight in volume.

Ten to 15 c.c. of serum are sufficient for single determination of the freezing-point, refractive index, specific gravity, protein content, and dry residue.

RESULTS. The results are given in the table on the opposite page. The cases are arranged in groups according to the clinical manifestations. The symptoms and serum pictures of each group will be discussed in detail.

GROUP I. *Normals.* Practising physicians and assistants in the hospital who were in good physical condition served as sources of normal serum.

Serum findings.	Freezing-point.	Δ Na $\times 10^2$	Specific gravity.	Dry residue.	Protein content.
Average	0.57	17.5	1.027	9.8	8.1

The individual variations from the average are very small, less than 4 per cent. in the freezing-point and refractive index, and less than 0.1 per cent. in the specific gravity. The average figures for the normals serve as a basis for comparison with the figures in the pathological groups.

GROUP II. *Cardiac Decompensation with Edema. Clinical Symptoms.* These cases all presented evidence of cardiovalvular disease with decompensation, many with a previous rheumatic history. All had hypertrophied *hearts*, five showing the characteristic enlargement of mitral disease, greatly displaced right heart and conus, and the sixth, mitral and aortic disease and a pericardial effusion which was confirmed by exploration. The *edema* varied from slight puffiness of legs to general edema of the dependent subcutaneous tissues, with fluid in the pleural and peritoneal cavities. The *urine* voided varied in volume from 600 c.c. to 2700 c.c.; average specific gravity, 1.016; all contained albumin in various amounts, and casts were found in 4 cases. The *eye-grounds* were normal in all of them. Five recovered sufficiently to leave the hospital and one died, and the diagnosis of mitral disease was confirmed at autopsy.

Serum findings.	Freezing-point.	Δ Na $\times 10^2$	Specific gravity.	Dry residue.	Protein content.
Average Group II	0.55	17.0	1.026	9.5	7.9
Average normal	0.57	17.5	1.027	9.8	8.1

The serum is practically normal. The individual variations are somewhat greater than in the normals, and the extremes in this group surpass the extremes in the group of normals. Yet these variations are insignificant. The general average of the group

corresponds closely to the normal average, but is slightly lower throughout.

GROUP III. *Chronic Nephritis with Edema. Clinical Symptoms.* All presented hypertrophy and dilatation of the *heart* to varying degrees. Systolic murmurs were noted in half the cases. The average blood-pressure was 130, with a maximum of 170 and a minimum of 110. The volume of *urine* varied from 600 c.c. to 3025 c.c.; average specific gravity, 1.019; they all contained albumin and casts; phthalein determinations were made in 4 cases:

1 H	First appearance noted in fifty-two minutes.
5 K	15 per cent. in first hour, 10 per cent. in second hour.
15 G	10 per cent. in first hour, 11 per cent. in second hour.
17 G	58 per cent. in first hour, 15 per cent. in second hour.

Edema was present in all cases, varying from pitting of the lower extremities to general subcutaneous edema and fluid in the serous cavities. Five cases showed varying degrees of neuroretinitis. No case presented any mental symptoms.

Serum findings.	Freezing-point.	Δ Na $\times 10^3$	Specific gravity.	Dry residue.	Protein content.
Average group III	0.56	13.2	1.020	7.6	5.9
Average normal	0.57	17.5	1.027	9.8	8.1

The serum in this group presents the characteristic picture of hydremia. With the exception of the freezing-point, all of the figures are much lower than normal. The serum is diluted. The normal values of the freezing-point show that the dilution is not due to water alone and that sufficient salt has also been retained to maintain the normal osmotic pressure.

GROUP IV. *Chronic Nephritis with Uremia. Clinical Symptoms.* The cases all presented very moderate degrees of cardiac hypertrophy. Systolic murmurs were noted in but 2 of the 6 cases. The average blood-pressure was 160, with a maximum of 190 and a minimum of 100. The urinary volume varied from 750 c.c. to 1650 c.c.; average specific gravity, 1.015; albumin was present in large amounts, and many casts were present; phthalein determinations were made in 5 cases:

2 P	Trace at the end of two hours.
3 C	None at the end of two hours.
4 L	None at the end of two hours.
5 K	16 per cent. in first hour, 14 per cent. in second hour.
60'S	16 per cent. in first hour, 3 per cent. in second hour.

Two of the cases presented very slight pitting of the skin over the tibiæ, but no fluid was present in the serous cavities. The *eye-grounds* were examined in 5 cases; 3 C and 4 L showed extreme neuroretinitis; in 2 P the retina was obscured by capacity of the

media; in 1 V the left eye was normal and the fundus of the right eye could not be seen; and 60'S was reported normal. Three of the 6 cases had *convulsions*, and all had *mental symptoms*, varying from restlessness and anxiety to active delirium finally resulting in coma and death.

Serum findings.	Freezing-point.	Δ Na $\times 10^2$	Specific gravity.	Dry residue.	Protein content.
Average group IV	0.67	18.0	1.029	11.0	8.4
Average normal	0.57	17.5	1.027	9.8	8.1

The serum of this group is characterized by a marked increase in the freezing-point and a slight increase in the other figures. This represents a concentrated serum with a relatively large increase in the concentration of the substances which affect the freezing-point.

GROUP V. *Chronic Nephritis with Uremia and Edema. Clinical Symptoms.* This group varies little from the last, except in the presence of edema of the extremities and the serous sacs. There was enlargement of the *heart* in all; dry pericarditis was noted in one of the cases. The average blood-pressure was 170, with a maximum of 200 and a minimum of 118. The urinary volume varies from 600 c.c. to 2200 c.c.; average specific gravity, 1.020; large amounts of albumin and many casts were present; phthalein determinations were made in 2 cases:

1 G Trace recovered in two hours.
3 C None recovered in two hours.

The *eye-grounds* in one case showed marked neuroretinitis (old and new); one was normal, and one case was not examined. All presented *mental symptoms* and had *convulsions*. One died, one became improved, and one well enough to discharge from the hospital.

Serum findings.	Freezing-point.	Δ Na $\times 10^2$	Specific gravity.	Dry residue.	Protein content.
Average group V	0.62	14.4	1.023	8.0	6.3
Average normal	0.57	17.5	1.027	9.8	8.1

The serum of this group presents a combination of the essential features of Groups III and IV. The freezing-point is increased and all other figures are lower than normal. This constitutes the paradox of a dilute serum with an abnormal increase in the concentration of the substances which affect the freezing-point.

The occurrence of this mixed form characterized by the coexistence of hydremia and an increased freezing-point is in thorough accordance with the results of metabolism studies on nephritics with impaired elimination of both salt (and water) and of nitrogen. Occasionally one symptom may dominate the picture to the exclusion of the others. In one of our cases not given in the table the

clinical symptoms and serum findings on admission indicated an advanced chronic nephritis with edema (Group II). As his condition progressed his edema gradually subsided until he became anhydropic, simultaneous with the development of uremic symptoms which terminated in coma and death. The changes in the clinical symptoms were accompanied by corresponding changes in the serum findings:

	Date.	Freezing-point.	Δ Na $\times 10^2$	Specific gravity.
Flan.	Oct. 6	0.53	14.1	1.024
	Oct. 28	0.61	16.6	1.027
	Nov. 1	0.67	18.4	1.030

Group VI. *Arteriosclerosis with Hypertension. Clinical Symptoms.* These cases all presented the same picture of high blood-pressure with cardiac hypertrophy and dilatation, loud aortic second sound, and no murmurs. The palpable vessels were all noted as thickened to varying degrees. The systolic blood-pressures were 190, 220, and 215. The volume of *urine* was good in all cases; average specific gravity, 1.020; small amounts of albumin were present, but no casts were noted; phthalein determinations were made on all:

1 G 27 per cent. in first hour, 24 per cent. in second hour.
2 H 30 per cent. in first hour, 21 per cent. in second hour.
3 W 60 per cent. in first hour, 19 per cent. in second hour.

In all cases large, tender livers were noted. There was slight edema over tibiæ in two cases, none in the third, and the serous cavities were free of fluid. The eye-grounds of two cases were examined; one was normal and the other showed moderate neuritis with tortuous vessels.

Serum findings.	Freezing-point.	Δ Na $\times 10^2$	Specific gravity.	Dry residue.	Protein content.
Average group VI	0.57	20.4	1.031	11.7	9.5
Average normal	0.57	17.5	1.027	9.8	8.1

This group is characterized by a marked increase in the concentration of protein in the serum. The freezing-point is normal, but all other figures are extremely high, chiefly on account of the increased concentration of serum protein.

Conclusions. The foregoing results demonstrate the practical value of this system of analysis in differentiating the cardiopathies from the nephropathies and in classifying the nephropathies. The diagnostic results thus obtained should correspond closely to the results obtained by a study of the metabolism balance. Determination of the freezing-point, refractive index, and specific gravity of blood serum is a simple procedure and requires at most two hours, while a study of the metabolism balance covering the same

ground would take at least a week. Analysis of serum by these methods possesses other advantages over the metabolism method. Retention of nitrogen or of water and salt is common to a variety of conditions, and is not necessarily indicative of nephritis. Serum analysis enables one to differentiate the cases in which retention is the result of defective renal elimination from those in which retention is due to other causes.

On the other hand there are limitations to the serum work. It is obvious that the retention of any substance must attain a certain threshold figure with respect to time and quantity before any changes could be detected in the serum by these methods. It is conceivable that a slight retention could be detected by the metabolism method before definite changes occurred in the serum. The metabolism method and serum analysis should be used to supplement each other until sufficient comparative data have been obtained.

It should also be borne in mind that the serum findings merely give a picture of the state of the serum at the time of examination. In pathological cases this picture may change from time to time with the progression or regression of the correlated symptoms. A uremic attack may clear up after several weeks either spontaneously or as a result of bleeding and restriction of protein in the diet, and the freezing-point may then return to normal. Similarly an hydremic serum may gradually change to normal during the disappearance of nephritic edema.

Serum analysis as well as the metabolism method also furnishes valuable indications as to the course of dietetic *therapy* to be followed in the different forms of nephropathies. In the uremic type a restriction of protein to the minimum necessary for maintenance is clearly indicated; at the same time the general nutrition should be kept up by increasing the fat and carbohydrate in the diet. In the hydropic form of nephropathy restriction of salt is indicated. Bleeding is beneficial in either uremic or hydropic cases. The restriction of salt or protein in the diet relieves the kidney of unnecessary work and rests the damaged function. No one would expect such treatment to remove scar tissue from the kidney or restore destroyed structures. It may be possible, however, to prevent a progression of the destruction of renal substance and to restore the function of partially damaged structures. At present it is impossible to foresee the beneficial results which may be derived from the dietetic treatment of early cases of chronic nephritis. It is not unreasonable to suppose that similar results would be obtained as in the rational dietetic treatment of diabetes.

THE RELATION BETWEEN FUNCTIONAL TESTS AND THE PATHOLOGICAL ANATOMY OF THE KIDNEY IN CHRONIC NEPHRITIS.

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Is it possible to tell during life what type of chronic nephritis from the pathologists' view-point is present in the individual case?

Before taking up that question it is important to define what is meant by chronic nephritis and what classification from the pathologists' view-point is the most satisfactory.

It seems most reasonable to consider as chronic nephritis any progressive destruction of the kidney parenchyma resulting from either some infectious agent or some bacterial, metabolic, or chemical poison. The process may start insidiously or follow some outspoken acute disturbance in the kidney. In some cases more than one cause may be present. In other cases a primary injury to the kidney by bacteria or other toxins may upon healing leave too little kidney substance to carry on renal function, so that gradually the remaining kidney tissue goes to pieces under the strain of its routine work. It must also be remembered that acute injury to the renal parenchyma may heal with scar formation and still have the remaining portions of the kidney function normally without any progressive degenerative changes starting in the kidney. Examples of such a condition vary from the isolated sclerosed glomeruli occasionally observed in children's kidneys up to the extensive scarring seen following acute bacterial infections which have healed. Such cases should be looked upon by both pathologist and clinician as healed nephritis and not chronic nephritis.

Although it is evident from the above that chronic nephritis covers a large field of renal conditions, this study will be simplified by leaving out of consideration those cases of chronic nephritis due to the presence of infective agents in the kidney. Certain of the cases reported may have been examples of a chronic nephritis starting upon the scarred kidney resulting from the healing of such an infection.

This work, therefore, narrows itself down to a consideration of those types of chronic nephritis which are usually met with in the medical wards of a hospital that come to a fatal termination. It must be remembered that the amount of kidney destruction in chronic nephritis varies considerably with the duration of the process, and that we rarely have a chance to study at autopsy the cases in the early stages of the progressive kidney disease.

In turning to a pathological classification for chronic nephritis one naturally meets most frequently the old terms chronic parenchymatous nephritis and chronic interstitial nephritis. The application of these terms to clinical conditions and in pathological studies has been rather loose. Furthermore, they do not suggest in the name what is the fundamental lesion in the kidney.

In Mallory's[1] recent book, the classification of nephritis for this group of cases is taken up from the view-point of what part of the kidney tissue is primarily involved. From the name, therefore, one may learn the original focus of the renal involvement, and from that realize just what has been going on in the kidney from the time of the original injury down to the end result.

Mallory, in this classification, speaks of tubular nephritis, capsular-glomerulonephritis, intracapillary-glomerulonephritis, and vascular nephritis. The lesions in any kidney may be of one type or a combination of several types. He mentions a variety of acute lesions which may occur in the first three of these types in that part of the kidney specified in the name. Some of these acute lesions heal without producing a permanent injury in the kidney. Many of them, however, on healing produce a permanent scar in the kidney with subsequent progressive degeneration of the renal parenchyma.

The types of acute nephritis which on healing are apt to turn into a chronic progressive nephritis are certain forms of the acute capsular-glomerulo and the acute intracapillary-glomerulo. It is the early stages of these types of progressive kidney destruction which are commonly considered clinically as chronic parenchymatous nephritis.

The chronic vascular nephritis usually results from simple arteriosclerosis of the smaller renal arteries, but may follow some acute lesion of the smaller renal vessels which upon healing causes impaired circulation with resulting progressive lesions in the vessels and renal parenchyma.

In the chronic vascular type secondary changes take place in the glomeruli supplied by the involved vessels, with eventual sclerosis of all or a part of the tuft. In the two glomerulo types usually the greater number of the glomeruli are involved, with eventual sclerosis of part or all of the capsules or tufts of both. In all three of the types following the injury to the glomeruli, secondary degenerative changes occur in the tubules. These may consist of atrophy and disappearance of the tubules or dilatation with atrophy of the lining epithelium.

Mallory is uncertain whether any actual proliferation takes place in the connective tissue of the kidney, but feels there is certainly a relative increase as the parenchyma disappears. The connective tissue is frequently invaded with cells of the lymphocytic series.

[1] Principles of Pathological Histology, 1914.

In this study the classification of nephritis suggested by Mallory has been followed, as it seems to be much more comprehensive than the older classifications. It was surprising how readily one could put the kidney into the proper group from examination of a single section under the microscope. Dr. Mallory has been kind enough to go over the slides and confirm the group into which each kidney belongs.

Up to the present time eighteen cases of chronic nephritis have come to autopsy at the Peter Bent Brigham Hospital, upon which enough clinical work has been done to make them of interest for comparison between the clinical and anatomical findings.

Unfortunately, as most of the cases were naturally seriously ill, it was not possible to put them on standard diets and learn their ability to put out added salt and urea which have been found at this hospital[2] to be of value in diagnosis and prognosis respectively of chronic nephritis. In most of the cases, however, the following four tests for diagnosis and prognosis of chronic nephritis were carried out: Examination of urine for albumin or casts, blood-pressure determinations, phenolsulphonephthalein excretion test, and estimation of non-protein nitrogen in the blood. In addition to reporting the results of these tests, record has been made of the age of the patient, the presence or absence of edema at the time of entrance, the examination of the eye-grounds, the previous acute infections, the result of the Wassermann serum reaction, and any complicating conditions at the time of death. This data was obtained from the medical records of the hospital.

It also seemed of interest to note the gross pathological findings at autopsy in order to see if it were possible to place these cases in their proper groups without the aid of the microscope. For this purpose the weight of the two kidneys, the width of the cortex, the adherence of the capsule, and the appearance of the surface of the kidney under the capsule were noted. This data was obtained from the pathological records of the hospital.

All this data is presented in the form of two tables, one containing the cases of chronic vascular nephritis, the other the cases of chronic glomerulonephritis. Most of the glomerulo cases were a combination of capsular-glomerulo and intracapillary-glomerulo. It is evident the majority of the cases are of the chronic vascular type.

Of the 14 cases considered as chronic vascular nephritis 1 was possibly a congenital malformation of the kidney and 2 were possibly healed acute infections which had involved other parts of the kidney besides the vessels and in which progressive renal destruction was going on. The weight of the kidneys varied from 360 grams to 42 grams. The capsule was adherent in 6 and stripped

[2] Frothingham, The Value of Certain Tests for Diagnosis and Prognosis in Chronic Nephritis, AMER JOUR. MED. SCI., June, 1915.

easily in 8. The surface of the kidney was granular or rough in 12 and smooth in 2. The cortex varied from 8 mm. to 1 mm. In the 4 cases of chronic glomerulonephritis one showed the process in its early stages probably not more than a few weeks or months. The weights varied from 435 grams to 155 grams. In 3 the capsule stripped easily, in 1 there was a slight resistance. The cortex varied from 11 mm. to 4 mm. The surface was smooth in 3 and granular in 1. It is thus evident that the kidneys can not be put with certainty into the proper group from the gross appearance alone. However, in the glomerulo type the capsule usually strips readily, leaving a smooth surface, while in the vascular type the surface is usually granular and the capsule more apt to be adherent.

All but 2 of the cases of chronic vascular nephritis showed albumin on the first or second examination of the urine, and these 2 occasionally did; 3 showed no casts on repeated examinations; 3 showed them only rarely, and the others showed casts pretty constantly. The blood-pressure on entrance in all cases but two was above 150 mm. of mercury. The pulse pressures varied from 100 to 40 mm.

In none of the 13 cases in which the 'phthalein test was done was the elimination for two hours above 40, and several showed no excretion in that time. The non-protein nitrogen of the blood was estimated in 11 of the cases, and in all but one was elevated above 30 mgm. per 100 c.c., which is considered normal when estimated by the Folin and Denis method. In some cases it went as high as 250+ mgm. per 100 c.c. of blood. These very high estimations were found in the blood usually just a short time before death, and probably represent a sudden terminal rise in non-protein nitrogen, which has frequently been noted in the last days of life in cases which have shown pronounced uremic symptoms for some time. Edema was present in 8 cases and absent in 6. In 6 of the 8 cases with edema, myocarditis was recorded as a complicating factor. In 5 of the 11 cases of chronic vascular nephritis in which eyegrounds were examined, no lesions were noted. In the other 6 there was edema, hemorrhages, or exudate, and in some all three. In 2 cases the Wassermann serum reaction was positive. In this group the ages varied from twenty-four to seventy-one years.

In the group of chronic glomerulonephritis albumin and casts were present in all cases. The blood-pressure was elevated above 150 mm. of mercury in 2 and not in the others. The pulse pressure varied from 80 to 45 mm. The phenolsulphonephthalein output was diminished in all 4 cases ranging from 22 in one and a half hours to 0 in two hours. In only 2 cases was the non-protein nitrogen of the blood estimated, and in those 2 it was above 100 mgm. per 100 c.c. Edema was present in 2 cases and absent in 2. In the 2 cases with edema there was no evidence of chronic cardiac

CHRONIC VASCULAR NEPHRITIS.

Hospital Med. No.	Kidney.				Age.	Urine.		Blood-pressure.		Pulse pressure.	Per cent. phthalein in 2 hrs.	Mgms. nitrogen per 100 c.c.	Edema.	Eye grounds.	Wassermann reaction.	Past acute infections.	Complications.
	Surface.	Wht. of both	Cortex	Capsule.		Albumin.	Casts	Systolic.	Diastolic.								
		Gm.	mm.														
328	Very rough	330	8.0	Adherent	61	+	+	170	110	60	31.0	–	+	No edema. No hemorrhage; no exudate	Not done.	Measles, pertussis, smallpox and acute rheumatism	Myocarditis.
673	Rough	195	4.0	Adherent	32	+	Rare	180	125	55	0	200	0	Not done	++	Measles. osteomyelitis with 7 operations	Fibrous pericarditis.
655	Rough	190	2.0	Strips easily	30	+	+	230	140	90	28.0	90	0	Hemorrhages; exudate; no edema	Negative	Dobie itch, dysentery, frequent tonsillitis, gonorrhea, malaria	None.
895	Granular	90	2.0	Strips easily	50	Rare	0	205	130	75	0	100	+	No edema; no hemorrhage; no exudate	Negative	Measles, chicken-pox, pertussis, bilious attacks	None.
1124	Finely granular	230	–	Strips easily	63	+	+	130	80	50	34.0	62	+	No edema; no hemorrhage; no exudate	Negative	Measles, mumps, pertussis, scarlet fever, acute rheumatism	Myocarditis; aortic insufficiency.
4	Rough	160	5.0	Slightly adherent	63	+	+	240	140	100	12.0	–	0	Exudate; no hemorrhage; no edema	Negative	None recorded	None.
1640	Granular	42	3.0	Adherent	24	+	0	120	68	52	0	204	0	No exudate; no hemorrhage; no edema	Negative	Measles, pertussis, chicken-pox, scarlet fever, sore throats	Possibly congenital malformation of kidney.
1593	Rough	90	1.0	Strips easily	31	+	+	238	138	100	3.0	56 to 138	0	Edema; exudate; hemorrhage	Negative	Measles, pertussis, chicken-pox, scarlet fever, typhoid. Convulsions at age (8–10)	None.
1975	Smooth	360	5.0	Strips easily	39	+	+	208	152	56	–	257.7	+	Edema; exudate; hemorrhage	Negative	Measles, erysipelas, typhoid	None.
1844	Rough	280	4.0	Slightly adherent	71	Rare	Rare	155	95	60	17.0	25	+	Not done	Negative	Measles, malaria	Myocarditis, auricular fibrillation, hemiplegia.
1405	Granular	340	3.5	Slightly adherent	59	+	Rare	175	130	45	40.5	–	+	Not done	Negative	Measles, acute rheumatism, gonorrhea, chancre	Myocarditis, auricular fibrillation, arteriosclerosis.

2006	Smooth	330	1.5	Strips easily	45	+	+	190	98	92	0	80	0	No edema; no exudate; no hemorrhages	+	Diphtheria, pneumonia scarlet fever, measles, whooping cough, mumps, typhoid	Marked amyloid in kidney glomeruli, myocarditis, mitral reguritation
2111	Granular	220	2.5	Strips easily	52	+	0	180	120	60	10.0	Urea 55.5	+	Slight edema; no hemorrhages; no exudate	Negative	Mumps, measles, pertussis, typhoid-pneumonia, broken arm	Myocarditis, arteriosclerosis, pericarditis.
2108	Granular	284	Markings vague	Strips easily	28	+	+	190	150	40	22.0	47.5	+	Edema; exudate; slight hemorrhage	Negative	Croup as a baby, moderate drinker up to 5 years ago. Dull red urine twice 6 yrs. ago.	Myocarditis, possibly old, healed intracapillary glomerulo lesion.

CHRONIC GLOMERULONEPHRITIS.

81	Smooth	435	11.0	Strips easily	26	+	+	140	85	55	22 in. 1½ hrs.	−	+	Not done	Not done	Chorea, some septic or tubercular chest condition, grippe	Pneumonia. Subacute nephritis of the intracapillary type.
251	Smooth	314	8.0	Strips easily	38	+	+	160	115	45	4.0	−	+	Slight edema; no hemorrhage; no exudate	Negative	Scarlet fever, typhus, rheumatic fever, ovary operation	Pericarditis, pleurisy, cystitis. Both intracapillary and capsular types.
1283	Granular	155	4.0	Slightly adherent	16	+	+	140	85	55	0	117	0	No exudate; no hemorrhage; no edema.	Negative	Measles, mumps, diphtheria, scarlet fever, chicken-pox, sore throats, pertussis	None. Both intracapillary and capsular types.
1860	Smooth	340	9.0	Strips easily	19	+	+	195	115	80	Trace	112	0	No edema; no hemorrhage; no exudate	Negative	Scarlet fever, measles, otitis media, frequent sore throats	None. Intracapillary type.

disease. In 3 of the cases of chronic glomerulonephritis the eye-grounds were studied, and except for slight edema in one no abnormal findings were noted. The Wassermann serum reaction was negative in the 3 cases in which it was done. The ages of these 4 cases ranged from thirty-eight to sixteen years, which is lower than those of the other group. There were, however, many cases of the vascular type within these age limits.

From a study of this small group of cases of chronic glomerulonephritis it is evident that it will not be possible by means of the four tests for renal disease mentioned above to tell definitely into which group a given case of nephritis belongs. The age of the patient, the presence or absence of edema or pulse pressure also does not give any assistance in this direction. Changes in the eye-grounds were not constant enough in either group to aid in classifying the cases. The previous history is not of assistance, for although most of the cases of glomorulonephritis had scarlet fever, still many of the cases of chronic vascular nephritis that died young also had had scarlet fever. It must be remembered that these cases are all ones of pronounced nephritis in the end stages. It is possible that by the more complicated dietary tests for renal function which may be carried out on the patients not so ill a grouping of the cases according to the pathological lesions may be accomplished. Possibly, therefore, at some future date enough of the chronic nephritis cases that have been studied in this hospital by these more elaborate methods will come to autopsy here to settle this question.

Grouping all these cases for clinical purposes simply as chronic nephritis of a severe grade, it is interesting to note that the non-protein nitrogen of the blood was elevated in all cases but one in which it was examined, and that one may well have died of cardiac and cerebral complications. The ability of the kidney to excrete phenolsulphonephthalein was diminished in all the cases in which it was done. Albumin was present in the first or second urine examinations in all cases but 2. Casts were not found in 3 cases and only rarely in 3 more. The blood-pressure was above 150 in all but 4 of the cases; 7 of the 14 cases in which the fundi were examined showed lesions in the eye-grounds.

THE RELATIONSHIP OF THE PATHOLOGICAL HISTOLOGY AND THE IODIN COMPOUNDS OF THE HUMAN THYROID.*

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and

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The present study presents some new evidence in the solution of the problems of the relationships between the clinical, pathological, and chemical findings in cases of human goitre. The scope of the study is limited to 566 cases, from which specimens have been analyzed chemically in the course of a general investigation of the iodin compounds of the thyroid. The cases were not selected, but were taken at random in the order as operated on from the patients under treatment in the Mayo Clinic during 1914.

Clinical Classification. The clinical classification of the cases into (1) hyperplastic toxic ("exophthalmic" goitre); (2) non-hyperplastic toxic with high blood-pressure; (3) non-hyperplastic toxic with low blood-pressure; (4) non-hyperplastic questionably toxic with low blood-pressure, and (5) non-hyperplastic atoxic with low blood-pressure has been made by Plummer,[1,2] and follows his previous grouping. Though the terms "hyperplastic" and "non-hyperplastic" refer to the morphology of the gland, which cannot be shown until its removal, yet they have been used in making the clinical diagnoses by Plummer and his associates with but a negligible margin of error, as shown by the subsequent pathological examination.

Pathological Classification. The pathological classification is, with slight modification, that previously published by Wilson.[3-10] The main divisions, (1) primary hypertrophy and hyperplasia of epithelium; (2) primary retention of colloid with atrophy of epithelium; (3) encapsulated adenomas, and (4) carcinomas, with their several subdivisions, are self-explanatory. As our study of the morphology of the thyroid in goitre has progressed, it has been found desirable to subdivide the group of regressing hyperplasias into subgroups, early, advanced, and very advanced regression. Also the undegenerated encapsulated adenomas, with colloid-filled acini, Group G, are so few in proportion to the degenerated adenomas, Group F, that in the present study the three subgroups have not been separated. The encapsulated adenomas have been separated from adenomatoses, and the latter

* Read before the Association of American Physicians, Washington, May 10, 1915.

included in the group described as primary retention of colloid with atrophy of epithelium.

CHEMICAL INVESTIGATION. The methods employed in the determination of iodin and the dry weight of thyroid substance removed at operation were as follows:

The fresh gland was placed in a crystallizing dish, covered with a glass plate, and heated three or four hours in an oven at 100° C. This preliminary treatment removed a large portion of the water and made the gland cut more easily into smaller pieces. After the gland was cut into small pieces it was completely dried in a vacuum desiccator, and then ground to a fine powder in a coffee mill, thoroughly mixed, and the iodin content determined[11] in a one-half gram portion. Two modifications of this procedure were employed for some of the glands. Instead of taking the entire fresh gland for purposes of desiccation, a known portion of the total was taken, and from the dried weight of this portion the dried weight of the total gland and the amount of iodin were calculated. The other modification consisted in taking a portion of the gland after it had been fixed in 4 per cent. formaldehyde. From this known portion the dried weight of the total gland was determined, and the total iodin based on this weight. Analysis of the formaldehyde solution showed that in every case an appreciable amount of iodin from the gland had passed into the formaldehyde solution. It was therefore necessary to determine the amount of iodin in this solution to obtain the total iodin originally present in the portion of the gland removed at operation. The results obtained by these procedures were kept separate until after they were compared with the pathological grouping. This comparison showed no appreciable differences between the three methods, so that in the final tabulation of results there was no discrimination made as to which method was employed for determining the total dried weight and the total iodin.

In addition to the determination of the total iodin, the dried thyroid substance of fifty-eight thyroids was hydrolized by a method already published.[13] This hydrolysis splits the proteins into simpler products and divides the total iodin into two chemically different groups. The α-iodin compound is insoluble in acids. The β-iodin compound is soluble. Both α- and β-iodin are in organic combinations, and there is evidence that β-iodin is not a decomposition product of the α-iodin compound, but that the two forms exist independently in the gland. Physiological tests[14] have shown that the α-iodin compound produces the typical effects of desiccated thyroid, but that the β-iodin compound has no toxic action. It therefore seemed desirable to determine the amount of α-, or toxic, iodin compound in some of the glands removed. For the determination of the amount of α-iodin in a given gland, the dry

powdered gland was boiled in 90 per cent. alcohol in the presence of 1 per cent. sodium hydroxide for forty-eight hours, 2.5 grams of the dried thyroid per 100 c.c. of alcohol. At the end of the boiling, carbon dioxide was passed through the solution and the alcohol evaporated. The solution was then acidified with 20 per cent. sulphuric acid. The precipitate (α-constituents) was filtered and washed with a small amount of water. This precipitate was dissolved in sodium hydroxide. The amounts of iodin in the filtrate (β-constituents) and in the solution of the α-constituents were determined. This gave the amounts of α- and β-iodin, and the sum of these two the total iodin in the gland.

In connection with the determination of iodin, it may be said that the results obtained during the course of this investigation approximate 4000 determinations of iodin. From a comparison of duplicates and an inspection of the accuracy of the total series, it would appear that for this work the method used is entirely adequate. The great advantage of obtaining a perfect "blank" where no iodin exists, of having no blue color flashed back from the starch iodin reaction after titration is finished, and the wide range in the amounts of iodin which come within the method, together with the shortness of time and inexpensive chemicals, have made this method the one of choice in our laboratory.

Protocols. The bulk of the material makes publication of protocols obviously cumbersome. However, the protocols of the chemical analyses and pathological examinations, with the microscopic sections, gross specimens and the clinical histories are on file in the Mayo Clinic, and are open to study to anyone interested. The results have been accurately compiled and condensed into a series of tables herewith presented.

Discussion of Tables. *Table I.* The distribution of the cases into the several clinical and pathological groups is given in totals, rather than in averages, that the numbers may serve as a basis for determining the percentage values in subsequent comparisons. It will be observed that the number of cases in certain groups (*A*, hyperplastic toxic; *D*, non-hyperplastic toxic and non-hyperplastic questionably toxic; *H*+*F*, non-hyperplastic toxic and non-hyperplastic questionably toxic; *F*, questionably toxic; and the carcinomas) are so small as to make the averages of relatively little value. However, it would have been more inaccurate to omit these cases entirely, and attention will be called to the insufficient evidence presented in these groups as the several comparative tables are discussed later. It should be noted that of the 425 cases of non-hyperplastic goitre, 197 presented symptoms which might have caused many of them to be diagnosed as "exophthalmic goitres" by clinicians elsewhere. Without analyzing in detail the distribution of these cases, it may be pointed out that the general distribution

GOITRES, CORRELATION OF PATHOLOGICAL, CLINICAL AND CHEMICAL DATA

TABLE I.—NUMBER OF CASES.

TABLE II.—AVERAGE AGES (IN YEARS).

PATHOLOGICAL CLASSIFICATION.	CLINICAL CLASSIFICATION. 1. Hyperplastic toxic ("exophthalmic" goitre).	2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).	3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).	4. Non-hyperplastic toxic(?) with low blood-pressure ("simple" goitre).	5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).	Totals (averages).	1. Hyperplastic toxic ("exophthalmic" goitre).	2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).	3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).	4. Non-hyperplastic toxic(?) with low blood-pressure ("simple" goitre).	5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).	Totals (averages).
1. PRIMARY HYPERTROPHY AND HYPERPLASIA OF EPITHELIUM:												
A. Early hypertrophy and hyperplasia	2	..	..	..	..	2	19	..	..	..	..	19
B. Advanced hyperplasia	44	..	..	..	..	44	34	..	..	..	..	34
C 1. Early regression of hyperplasia	38	..	..	..	..	38	38	..	..	..	..	38
C 2. Advanced regression of hyperplasia	36	..	..	..	..	36	35	..	..	..	..	35
C 3. Very advanced regression of hyperplasia	17	..	..	..	..	17	34	..	..	..	..	34
2. PRIMARY RETENTION OF COLLOID; ATROPHY OF EPITHELIUM:												
D. Secondary regeneration of epithelium	4	16	5	4	25	54	29	45	40	33	32	32
H. Diffuse atrophy of epithelium	..	65	35	11	96	207	..	50	37	35	35	40
H + F. Diffuse atrophy of epithelium with included adenomas	..	27	9	2	47	85	..	49	33	38	36	40
3 ENCAPSULATED ADENOMAS: E, F, G	..	25	12	7	35	79	..	46	40	44	36	40
4. CARCINOMAS	..	3	—	—	1	4	..	44	—	—	42	44
Totals (average)	141	136	61	24	204	566	35	49	38	38	35	39

closely approximates that shown in a similar group of patients operated on in 1911 and 1912.[9]

Table II. Table II shows the average age of the patients at the time their thyroids were removed. While the average ages of the patients with hyperplastic toxic goitre is thirty-five years, it will be noted that the average age of those with early hypertrophy is only nineteen years, of those with advanced hyperplasia thirty-four years, and of those whose thyroids showed regression in the hyperplastic process it is thirty-eight, thirty-five and thirty-four years respectively, in inverse order to the amount of regression. At first thought, it would appear that this inversion of the average ages in relation to the amount of regression of hyperplasia is contradictory, but when the average ages are examined in the light of Table III, in which is shown the average duration of goitre in months, it will be seen that while the younger patients showed the greatest amount of epithelial regression the duration of the goitre as well as the duration of symptoms were both also inversely as to age and directly as to the amount of regression. The same holds good in the four cases of clinically hyperplastic toxic goitre with secondary regeneration of the thyroid epithelium. Here the average age was twenty-nine years, and though the average duration of goitre was one hundred and thirty-two months, the average duration of symptoms was only eleven months. In this pathological group (epithelial regenerations) the age-distribution of the patients in the various clinical classes is interesting, being twenty-nine years in the hyperplastic toxic, forty-five years in the non-hyperplastic toxic with high blood-pressure, fifty years in the non-hyperplastic toxics with low blood-pressure, thirty-three years in the non-hyperplastic questionably toxic, and thirty-two years in the non-hyperplastic atoxic cases.

The somewhat erratic age distribution of the cases in which the glands showed encapsulated adenomas, either alone (*E*, *F*, *G*) or included in diffuse colloid goitres (*H*+*F*), may not be wholly accidental, but may be due to the influence of the neoplasms. This point, however, is still under investigation in a larger series of cases.

Table III. The average duration of goitres in months for the entire series and the duration of hyperthyroidism in months for the hyperplastic series is shown in Table III. The duration of the symptoms in the toxic non-hyperplastic cases is so difficult to determine with any degree of accuracy from the patient's description that no attempt has been made to state it in months. The difference between the period of duration of goitre in hyperplastic toxics, averaging forty-one months, and the period of duration of goitre in the non-hyperplastic groups (the lowest of which is 156 months, and the highest 276 months, with an average of 192 months) is very marked, and constitutes a point in clinical diagnosis.

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TABLE III.—AVERAGE DURATION OF GOITRES AND AVERAGE DURATION OF TOXIC SYMPTOMS (IN MONTHS).

TABLE IV.—AVERAGE SYSTOLIC BLOOD-PRESSURE.

PATHOLOGICAL CLASSIFICATION.	CLINICAL CLASSIFICATION. 1. Hyperplastic toxic ("exophthalmic" goitre).	2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).	3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).	4. Non-hyperplastic toxic(?) with low blood-pressure ("simple" goitre).	5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).	Totals (averages).	1. Hyperplastic toxic ("exophthalmic" goitre).	2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).	3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).	4. Non-hyperplastic toxic(?) with low blood-pressure ("simple" goitre).	5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).	Totals (averages).
PRIMARY HYPERTROPHY AND HYPERPLASIA OF EPITHELIUM:												
A. Early hypertrophy and hyperplasia . .	9 (9)	..	..	..	..	9 (9)	140	..	..	..	..	140
B. Advanced hyperplasia	17 (10)	..	..	..	..	17 (10)	138	..	..	..	..	138
C 1. Early regression of hyperplasia . . .	32 (18)	..	..	..	..	32 (18)	147	..	..	..	..	147
C 2. Advanced regression of hyperplasia . .	53 (35)	..	..	..	..	53 (35)	132	..	..	..	..	132
C 3. Very advanced regression of hyperplasia	68 (47)	..	..	..	..	68 (47)	144	..	..	..	..	144
PRIMARY RETENTION OF COLLOID; ATROPHY OF EPITHELIUM:												
D. Secondary regeneration of epithelium .	132 (11)	216	276	204	156	209	148	164	129	120	125	140
H. Diffuse atrophy of epithelium . . .	..	240	180	240	168	204	..	171	130	128	120	141
H + F. Diffuse atrophy of epithelium with included adenomas	..	216	156	240	168	180	..	176	121	132	124	143
3. ENCAPSULATED ADENOMAS: E, F, G	..	180	180	192	156	168	..	171	129	126	128	144
4. CARCINOMAS	..	192	—	—	300	252	..	157	—	—	120	142
Totals (averages)	41	228	180	216	168		143	171	128	127	123	

The maximum severity of symptoms, and the severity at the time of examinations in the several groups of hyperplastic toxic cases, indicated on a scale of 1, 2, 3, 4, and 5, averaged as follows:

		Maximum severity.	At time of examination.
A	Early hypertrophy	1.0	1.0
B.	Advanced hyperplasia	2.6	2.5
C 1.	Early regression	3.2	2.4
C 2.	Advanced regression	3.6	2.5
C 3.	Very advanced regression	3.4	2.0

Table IV. The discussion of the systolic blood-pressure as presented in Table IV will be covered *in extenso* by Plummer.[16] It is included in the present paper only for reference in relation to the percentage of iodin and total amount of iodin in the portion of removed gland. (See Tables VI and VII.)

Table V. The average weight of the portion of the gland removed at operation in the hyperplastic toxic group was 57 grams, as compared with 55 grams, the average weight of the removed portion in the 1911 and 1912 cases.[9] The average weight of the removed portion of the 425 cases of non-hyperplastic thyroids was 168 grams, as compared with 171 grams, the average weight of the non-hyperplastics in the 1911 and 1912 series.[9] This is of significance in showing the great desparity in size between the thyroids from hyperplastic toxic and those from non-hyperplastic toxic cases as previously noted.[3 9] In the individual groups the removed portion of gland is larger in the cases of high blood-pressure than in the several pathological groups with low blood-pressure.

Table VI. The variation in the percentage of iodin in the dried gland in the several histological types of thyroids from hyperplastic toxic cases is most marked. Starting in with the cases of early hypertrophy, the percentage is 0.11. It drops thence to 0.03 in the advanced hyperplasias, rises to 0.07 in the early regressions, to 0.16 in the advanced regressions, and to 0.19 in the very advanced regressions. A comparison of these percentages with those showing percentages of iodin in the various non-hyperplastic thyroids shows that in no subgroup of the latter division does the percentage of iodin rise as high as that in the thyroids from cases with advanced regression in hyperplastic glands.

In the pathological groups of the non-hyperplastic series the secondary regenerations (type D) present both the highest and the lowest percentages aside from certain low averages in the encapsulated adenomas and the carcinomas. The diffuse epithelial atrophies (type H) vary the least. The encapsulated adenomas while generally low vary from 0.02 to 0.07.

In the individual clinical groups, it is interesting to note that in all, except the adenomas, the percentage of iodin is highest (av. 0.1 per cent.) in the non-hyperplastic toxic cases with low blood-pressure. The next in amount are the cases of non-hyperplastic toxic with high blood-pressure (av. 0.08 per cent.). In general,

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TABLE V.—AVERAGE WEIGHT OF REMOVED GLAND (FRESH) IN GRAMS.

TABLE VI.—AVERAGE PER CENT. OF IODIN IN DRIED THYROID.

PATHOLOGICAL CLASSIFICATION.	CLINICAL CLASSIFICATION:	1. Hyperplastic toxic ("exophthalmic" goitre).	2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).	3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).	4. Non-hyperplastic toxic(?) with low blood-pressure ("simple" goitre).	5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).	Totals (averages).	1. Hyperplastic toxic ("exophthalmic" goitre)	2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).	3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).	4. Non-hyperplastictoxic (?) with low blood-pressure ("simple" goitre).	5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).	Totals (averages).
1. PRIMARY HYPERTROPHY AND HYPERPLASIA OF EPITHELIUM:													
A. Early hypertrophy and hyperplasia		46	..	..	..	..	46	0.11	..	..	..	..	0.11
B. Advanced hyperplasia		59	..	..	..	..	59	0.03	..	..	..	..	0.03
C 1. Early regression of hyperplasia		56	..	..	..	..	56	0.07	..	..	..	..	0.07
C 2 Advanced regression of hyperplasia		53	..	..	..	..	53	0.16	..	..	..	..	0.16
C 3. Very advanced regression of hyperplasia		70	..	..	..	..	70	0.19	..	..	..	..	0.19
2. PRIMARY RETENTION OF COLLOID ATROPHY OF EPITHELIUM:													
D. Secondary regeneration of epithelium		42	175	146	151	171	159	0.07	0.08	0.14	0.05	0.05	0.07
H. Diffuse atrophy of epithelium		..	223	169	170	158	181	..	0.08 −	0.11 −	0.08	0.08 −	0.08 +
H + F. Diffuse atrophy of epithelium with included adenomas		..	189	112	266	183	179	..	0.09	0.12	0.05	0.06	0.07
3. ENCAPSULATED ADENOMAS:													
E, F, G		..	109	125	140	108	114	..	0.07	0.02	0.04	0.06	0.06
4 CARCINOMAS		...	730	−	−	140	583	..	0.005	−	−	0.07	0.02
Totals (averages)		57	190	150	167	157	137	0.10	0.08	0.10	0.06	0.06+	0.085

the percentage is lowest in the non-hyperplastic atoxic (av. 0.06 per cent.). Attention is called to this inversion of the order of the percentage amounts in relation to clinical symptoms over those observed in the cases of hyperplastic goitre.

A tabulation of both groups of non-hyperplastic toxic cases in comparison with the non-hyperplastic atoxic cases shows that in 84 per cent. of the atoxic the percentage of iodin was under 0.1, while but 68 per cent. of the toxic cases were under 0.1.

Table VII. In the hyperplastic toxic cases, the total amount of iodin in the portion of the gland removed follows the percentage of iodin since the portion of gland removed in these cases is fairly equal in the several groups. The amount averages 9.2 mg. in early hypertrophy, drops to 3.4 mgs. in the advanced hyperplasias, rises to 8 mgs. in the early regressions, to 14.2 mgs. in the advanced regressions, and to 21.9 mgs. in the very advanced regressions. The total amount in the cases with secondary regeneration of epithelium, which showed symptoms placing them in the hyperplastic toxic clinical group, is the smallest of any of the groups except the advanced hyperplastic toxics and carcinomas.

In the non-hyperplastics, the largest amount is in the toxics with low blood-pressure (23.8 mgs.), while in the atoxics the amount averages 15 mgs. It should be noted that though the amount of iodin in the portions of glands removed in the non-hyperplastic cases is greater than the amount removed in the hyperplastic cases, the comparison of the relative amounts in the total gland is not made on the same basis, since in the non-hyperplastics a very much larger proportion of the gland is removed at operation (frequently as much as $\frac{9}{10}$) than is removed at operation in hyperplastic cases (rarely more than $\frac{2}{3}$).

Thus, it is probable that the total amount of iodin in the entire gland in the cases of hyperplastic goitre with very advanced regression averages more than the total amount of iodin in the entire gland in the non-hyperplastic cases.

The averages of the total iodin of patients grouped as to age by half-decades shows no order or regularity, but a similar grouping of the average total amounts of iodin arranged by duration of goitre in half-decades results as follows:

ADDENDUM TO TABLE VII.—TOTAL IODIN AND DURATION OF GOITRE.

Duration of goitre in half-decades.	Non-hyperplastic toxic. Number of cases.	Non-hyperplastic toxic. Average total iodin, mgs.	Non-hyperplastic atoxic. Number of cases.	Non-hyperplastic atoxic. Average total iodin, mgs.
5−	30	19.6	23	13.7
5+	21	18.4	37	12.3
10+	26	21.3	28	16.9
15+	23	32.9	30	16.9
20+	22	28.3	20	22.5
25+	19	22.3	11	14.0
30+	12	22.1	1	13.5
35+	8	28.3	2	16.2
40+	11	28.3	3	16.0

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TABLE VII.—TOTAL IODIN IN PORTION OF GLAND REMOVED (IN MILLIGRAMS).

PATHOLOGICAL CLASSIFICATION.	CLINICAL CLASSIFICATION. 1. Hyperplastic toxic ("exophthalmic" goitre).	2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).	3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).	4. Non-hyperplastic toxic(?) with low blood-pressure ("simple" goitre).	5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).	Totals (averages).
1. PRIMARY HYPERTROPHY AND HYPERPLASIA OF EPITHELIUM:						
A. Early hypertrophy and hyperplasia	9.2	..	..	..	..	9.2
B. Advanced hyperplasia	3.4	..	..	..	..	3.4
C 1. Early regression of hyperplasia	8.0	..	..	..	..	8.0
C 2. Advanced regression of hyperplasia	14.2	..	..	..	..	14.2
C 3. Very advanced regression of hyperplasia	21.9	..	..	..	..	21.9
2. PRIMARY RETENTION OF COLLOID; ATROPHY OF EPITHELIUM:						
D. Secondary regeneration of epithelium	5.7	19.9	25.6	11.9	12.1	14.9
H. Diffuse atrophy of epithelium	..	28.1	32.8	21.1	18.4	23.9
H + F. Diffuse atrophy of epithelium with included adenomas	..	27.5	22.2	11.1	13.0	18.6
3. ENCAPSULATED ADENOMAS: E, F, G	..	13.8	11.6	6.4	10.0	10.9
4. CARCINOMAS	..	5.1	—	—	1.6	4.4
Totals (averages)	9.7	23.8	26.5	14.5	15.0	

TABLE VIII.—AVERAGE PERCENTAGE OF α-IODIN (Number of determinations shown in parenthesis).

1. Hyperplastic toxic ("exophthalmic" goitre).	2. Non-hyperplastic toxic with high blood-pressure ("simple" goitre).	3. Non-hyperplastic toxic with low blood-pressure ("simple" goitre).	4. Non-hyperplastic toxic(?) with low blood-pressure ("simple" goitre).	5. Non-hyperplastic atoxic with low blood-pressure ("simple" goitre).	Totals (averages).
7 (1)	..	..	..	..	7 (1)
16 (11)	..	..	..	..	16 (11)
31 (8)	..	..	..	..	31 (8)
31 (6)	..	..	..	..	31 (6)
37 (4)	..	..	..	..	37 (4)
—	—	16 (1)	—	34 (1)	25 (2)
..	30 (2)	33 (4)	38 (1)	35 (6)	34 (13)
..	—	25 (1)	—	18 (1)	22 (2)
..	46 (1)	27 (2)	—	35 (8)	34 (11)
..	..	..			
25 (30)	36 (3)	28 (8)	38 (1)	34 (16)	(58)

While there are considerable fluctuations in the total amount of iodin present at the different half-decades, the most constant relationship is that at each half-decade the total amount in the toxic cases is materially more than is the total amount in the atoxic cases.

Table VIII. The determination of the α-iodin has been made in too few cases to make the average percentages of much comparative value, there being but 30 cases in the hyperplastic group and 28 in the non-hyperplastic group. It may, however, be noted that in those groups in which a sufficient number of cases exist for comparison, that the following order is presented: In the cases of advanced hyperplasia, the percentage of the total iodin in the α form is 16 (11 cases), and rises to 35 (18 cases) in the advanced regressions. In the non-hyperplastic cases, if the two groups with toxic symptoms are placed together (11 cases), the average percentage of the total iodin in the α form is 30, while in the atoxic group (16 cases) the average percentage is 34. Thus it will be seen that there is a parallel relationship in the two groups, though until further data is obtained no great significance can be attached to it.

General Discussion. 1. The data herein presented furnishes additional proof of the statements previously made by one of us,[3] that the symptom complex, which is generally recognized as "typical Graves's disease," "exophthalmic goitre," etc., and sharply denoted by Plummer as hyperplastic toxic goitre is constantly parallel in all its stages of development and regression with similar stages of development and regression in the parenchyma of the thyroid. This parallelism is shown in the average duration of goitre, the average duration of toxic symptoms, and in the progressive and regressive histological changes.

Now, for the first time in detail the percentages and total amounts of iodin, the pathological groups, and the clinical types have been compared in the same series of cases. As previously suggested by the work of Smith and Broders,[15] a close parallelism obtains throughout the data from the three sources.

From previous investigations there seemed to be little doubt that the clinical picture of exophthalmic goitre is produced, either directly or indirectly, by hyperactivity of the thyroid; but until some definite substance had been isolated from the normal thyroid and from the pathological glands and shown to be toxic in its nature, no final conclusion could be arrived at. The isolation in pure form of a compound containing 60 per cent. of iodin[12 13 14] and the proof that this substance is highly toxic in nature, emphasized the importance of an investigation concerning the amount and nature of the iodin-containing compounds of the thyroid. It has been shown that the iodin in the glands exists in two independent forms of combination, only one of which, the α form, is toxic. We must therefore enlarge our conception of the physiological action of the iodin compounds

to include the action of this one the toxicity of which is vastly greater than that of any other hitherto described.

It is significant to find that this α-iodin compound is present in the actively hyperplastic glands of advanced hyperplastic toxic goitres in only $\frac{1}{20}$ to $\frac{1}{15}$ the amount in which it is present in normal thyroids. This must be interpreted not as a reduced production of the toxic substance but as the result of its greatly increased diffusion from the gland into the blood stream. There is no quantitative measure of the secretory activity of the thyroid, but its storage capacity for the toxic substance is obviously proportional to its iodin content. If further observations support the relatively few herein recorded, it would seem to be a fair assumption that the α-iodin compound is responsible for the toxic symptoms in hyperplastic toxic goitre. The constant direct relationship between the clinical symptoms and pathological picture and the reservoir capacity of the thyroid in hyperplastic toxic goitre is strikingly shown in Tables VI, VII, and VIII. The failure on the part of other pathologists to recognize this constant association, we believe, has been due (1) to failure by clinicians to distinguish sharply between hyperplastic toxic goitre ("typical acute exophthalmic," "Graves's disease," etc.) and the several indeterminate groups of non-hyperplastic toxic goitre ("atypical chronic Graves's disease," "cardiovascular goitre," etc.), and (2) failure to recognize the fact long ago suggested,[3] that the chemical constituents found in the thyroid are only the complement of those which must have gone out of the gland to have caused symptoms.

2. The relationships of the pathology and chemistry of non-hyperplastic thyroids to the various clinical groups of toxic and atoxic non-hyperplastic goitre are still far from being cleared up. This is due (1) to the difficulty in accurately grouping these cases clinically, (2) to the difficulty in securing accurate information as to the onset and course of the chronic symptoms, and (3) to the difficulty in intrepreting long past primary pathological changes in the light of present pathological and chemical findings since most of these patients seek surgical aid many years after the beginning of the goitre, and probably also several years after the beginning of symptoms. That the relationship of the histological changes in the thyroids designated as epithelial regenerations is parallel with the iodin content of the glands, and to some extent with the clininal history of the patients from whom the glands were removed, is shown in the several tables.

One fact running through all the tables is that the amount of iodin in the gland parallels the clinical grouping. In the actively hyperplastic glands (group B) it has been shown that the amounts of iodin and α-iodin are very low, but in cases where regression has occurred (group C) the amounts of iodin are high. In contrast to this it was found that the amount of iodin in the non-hyperplastic toxic glands is higher than in the non-hyperplastic atoxic glands.

The clinical picture, in its most severe type, of patients with non-hyperplastic toxic goitre approaches in many respects the picture of patients with hyperplastic toxic goitre. Assuming the same toxic substance to be the cause for all thyroid intoxication, the factors involved to produce varying clinical pictures, are the daily amount of absorption of the toxic substance, the length of time during which this intoxication occurs, and the personal resistance of the patient. At present we have no conclusive evidence explaining the higher iodin content of toxic non-hyperplastic glands than that of the actively toxic hyperplastic glands, but it seems probable that the diffusibility from the gland of the α-iodin compound may be an important factor in determining whether a goitre produces toxic symptoms or not.

Further rearrangements of the clinical groups of non-hyperplastic goitre are in progress by Plummer, and further studies of the pathology and chemistry of the thyroids from these cases are now being made by us and will be reported later.

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STUDIES ON THE URIC ACID IN THE BLOOD IN GOUT. SECOND PAPER.

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It is now known that uric acid is constantly present in demonstrable amounts in the blood of man. In 38 patients at the Boston Psychopathic Hospital, Folin and Denis[1] found that the amount of uric acid in the blood determined by their newly discovered colorimetric method varied from 0.7 to 3.7 mgs. of uric acid per 100 grams of blood. Adler and Ragle[2] recently reported the findings in 156 patients examined in the same hospital. The uric acid ranged from 0.7 mgs. to 4.5 mgs. per 100 grams of blood. In 107 out of the 156 cases the amount was between 1 and 2 mgs. In 11 cases there was less than 1 mg. and in 38 cases more than 2 mgs. These cases in both series were unselected. The blood was obtained from newly admitted patients taken seriatim and doubtless included somatic diseases, especially chronic interstitial nephritis, arteriosclerosis, and alcoholism. When classified according to the psychiatric diagnosis, the slight variation in the average amount of uric acid found in each group is striking. The lowest average amount was 1.31 mgs. found in 6 cases of general paresis, the highest, 1.86 mgs. in epileptic insanity, of which disease, however, there was only one case. Adler and Ragle concluded that the blood of insane patients contained the normal amount of uric acid on an ordinary diet. This is probably correct. They are the only figures based on a large number of analyses available for forming even an approximation of the variations in the amount of uric acid that is present in the blood of healthy individuals on an ordinary diet.

The view was held until recently that uric acid was not demonstrable in the blood of normal individuals on a purin-free diet. Its constant occurrence with the patient on this diet was regarded as a characteristic feature of gout, and diagnostically important.[3]

McLester,[4] using Folin's method, found uric acid in the blood of fifteen normal individuals who had been on a purin-free diet, for at least three days, in amounts ranging from 0.5 to 2.9 mgs. per 100 grams of blood. A study of his table shows that the average amount was 1.4, while the figures given by Adler and Ragle show that the average amount in their 156 cases was 1.7. That these amounts so nearly agree, deserves to be emphasized, especially as nearly all the individuals studied by McLester were young, healthy adults on a purin-free diet, while the patients studied by Adler and Ragle were of all ages and on a mixed diet.

Very different from these figures are those obtained in gout. In 1913 I reported 11 cases of typical gout in which the uric acid in the blood had been determined by the method of Folin and Denis in Folin's laboratory.[6] At the present time the number of cases studied has been increased to 16. The analyses during the past two years were made by Mr. Ragle and myself in the laboratory of the Psychopathic Hospital. Only those cases are included (1) in which tophi were found; (2) in which a history of characteristic attacks of acute gout was obtained; or (3) in which typical symptoms developed while under observation.

The average amount of uric acid irrespective of the diet or the condition of the patient at the time of the examination was 3.7 mgs. Three of the patients seen during attacks were on an ordinary mixed diet. They had 4.5 mgs., 4.8 mgs., and 5.7 mgs. of uric acid. In the blood of two other patients examined during an attack while on a purin-free diet the uric acid in four determinations ranged from 2.4 to 5.1 mgs., with an average amount of 3.6 mgs. None of these patients was taking atophan.

Seven patients were examined at a time when they were free from symptoms of gout and when they were on a mixed diet. Their blood contained from 3.1 mgs. to 5.5 mgs. The average was 4.3 mgs. In the blood of six patients on a purin-free diet examined at a time when they had no acute manifestations of gout the uric acid ranged from 1.6 to 7.2 mgs., with an average of 3 mgs. These figures show that in the cases studied there was more uric acid in the blood when on a mixed diet both in the interval and during attacks than when on a purin-free diet. In all, twelve examinations were made when a mixed diet was taken during attacks as well as in the intervals, and the average amount of uric acid was 4.3 mgs. Adler and Ragle, as already stated, obtained an average amount of 1.7 mg. in their 156 unselected psychiatric cases on a mixed diet. A comparison of these two figures shows that there is usually in gout a marked hyperuricemia. In the cases examined there was more than twice as much uric acid on the average than in the blood of non-gouty cases. The same conclusion is reached by taking all the analyses upon which this study is based without regard to the diet, medicines taken, or the condition of the patient at the time of the examination. Thirty-eight determinations were made on sixteen cases of gout, and the average amount of uric acid was 3.7 mgs. per 100 grams of blood.

On a purin-free diet the average amount was larger during an attack than during the interval—in the former 4.3 mgs., in the latter 2.4 mgs. The number of cases is too small to warrant the conclusion that in gout there is usually more uric acid present in the blood during an attack than at other times. That this is the rule, however, is at least suggested by the analysis of all the cases without regard to diet, whether ordinary or purin-free. Eight determina-

tions were made on six patients during an attack, and the average amount of uric acid was 4.6 mgs. Eighteen estimations were made on twelve cases when free from acute symptoms of gout, and 3.3 mg. was the average concentration.

Although these analyses and those of other investigators show that the blood in gout usually contains a relatively large amount of uric acid, the diagnosis of gout cannot be based solely on this finding, as a high concentration is sometimes found in other joint conditions; but in these the hyperuricemia has been transitory, while in gout it is usually constant. In a case of infectious arthritis which did not have the clinical features of gout, the uric acid in the blood at the first examination was 7.6 mgs. The analysis was made by Dr. Denis. Seven months later the blood was again analyzed and only 0.8 mg. was found, although the patient at the time was on a diet rich in purins. Other similar cases have shown the value of repeated blood examinations.

In typical gout the uric acid may be low at times, even when atophan has not been taken. In one of my patients the first analysis showed only 1.7 mg. of uric acid (purin-free diet), and in the blood of another case on a mixed diet there was 1.9 mg.

In the sixteen cases of gout studied no relation could be traced between the amount of uric acid in the blood and the severity or character of the disease. Two of the patients had many large deposits of sodium urate beneath the skin in different parts of the body. The blood of both contained less than the average amount of uric acid found in gout—one had 2.4 mgs. on a purin-free diet, the other 2.2 mgs. These findings show that the presence of many tophi is no indication that hyperuricemia exists.

The amount of uric acid in the blood bears no apparent relation to the age of the patient.

A considerable variation in the uric acid content may be found in the blood of the same individual within a short time which cannot be attributed to purin in the food. In my first paper I called attention to this fact. A patient admitted in a severe attack of gout had only 2.7 mgs. of uric acid in his blood at the first examination made only twenty-four hours after the purin-free diet was begun. Later the blood contained 5.1 mgs., and he had been fed no food containing purins for fifteen days.

It is not known whether or not the uric acid concentration varies considerably in healthy individuals on a purin-free diet, as sufficient observations on this point are lacking. McLester made four examinations on one healthy person who was on a purin-free diet, and the amount of uric acid was practically constant. But in some cases of gout the variation in the blood at different times may be slight. I examined one case in which the amount of uric acid was unusually low—there was 1.7 mg. present. Nearly two years later a second examination was made and 1.3 mg. found.

That two of the lowest amounts of uric acid yet recorded in gout, both well within the limits of normal, with a long interval between the tests, were obtained from the same patient indicates that the concentration of uric acid in the blood of gout may in some cases be fairly constant.

On the other hand, individuals who have no symptoms or signs of gout may have a wide variation in the uric acid content of the blood. For example, M., a patient with recurrent iritis, had 2.2 mgs. after having been on a purin-free diet for two days. A few months later when on a mixed diet his blood contained only 0.8 mg.

Great fluctuations in the amount of uric acid independent of diet are sometimes observed. This was strikingly shown in a case of primary polyarthritis. (See Table I.)

TABLE I

		Mgs. of uric acid per 100 grams of blood.
McC., aged twenty-two years.		
October.	Ordinary diet	2.7
December.	Purin-free diet	5.0
May.	Purin-free diet	1.6

In another case of chronic non-gouty arthritis the blood at the time of the first analysis contained 7.6 mgs. of uric acid. A few months later when on a diet rich in purins only 0.8 mg. was found.

After feeding five gouty patients a meal rich in purins I have observed a marked rise in the uric acid content of the blood above the upper limit of normal. (See Table II.)

TABLE II

	Mgs. of uric acid in 100 gms. of blood.		Mgs. of uric acid in 100 gms. of blood.
D. N. Gout. Purin-free diet	3.1	52 hours after eating 280 gms. haddock roe	5.8
		3 days after eating 300 gms. roast beef	6.2
K. Gout. Purin-free diet	2.4	24 hours after eating 270 gms. roast beef	3.0
H. Gout. Purin-free diet	1.7	3 days after eating 150 gms. thymus	3.6
P. Gout. Purin-free diet	2.1	3 days after eating 160 gms. thymus	3.4
J. N. Gout. Purin-free diet	2.2	48 hours after eating 190 gms. thymus	8.7
Average	2.2	Average	5.1

In four cases of gout in which the uric acid concentration at the first examination was below the upper limit of normal, 2.5 mgs., the blood after this test meal contained a large amount of uric acid.

In the investigation of my first two cases I fed roast beef, but

subsequently used sweetbreads for the purin test meal. The patients were placed on a purin-free diet for several days and then a meal of sweetbreads was given. The amount taken ranged from 150 to 300 grams (raw weight). If the patient did not eat the amount ordered at one meal the remainder was given at the following meal. After feeding the sweetbreads the purin-free diet was resumed. The blood was examined after intervals of time ranging in different cases from twenty-four hours to four days. In the three cases of gout tested there was a striking increase in the amount of uric acid in the blood one to three days after the sweetbread meal. In one case after feeding 190 grams of thymus gland the amount of uric acid in the blood was doubled in the first twenty-four hours, rising from 2.2 mgs. to 4.4 mgs. On the third day it reached a maximum of 8.7 mgs. On the fourth day it fell to 2.7 mgs.

This marked disturbance in the uric acid metabolism was not indicated by any apparent delay or diminution in the output of the exogenous purin in the urine; 26.2 per cent. of the ingested purin nitrogen was excreted as uric acid. Burian and Schur[7] found in a normal individual only 25 per cent. of the purin nitrogen of calves' thymus excreted in the urine as uric acid, while a healthy man studied by Pollak put out as uric acid only 15 per cent. of the exogenous purin nitrogen. In the case just cited if the increased output of uric acid comes from the purin bases contained in the sweetbreads then 26.2 per cent. of the ingested purin nitrogen was excreted as uric acid, and this is more than Burian and Schur[7] obtained in a normal individual. It has been demonstrated by Vogt,[9] Reach,[10] Soetbeer,[11] Pollak,[8] Mallory[12], and others that in gout the excretion of exogenous purin is diminished and delayed. That this is not invariably the case was pointed out recently by Magnus Levy,[13] and our study of the blood shows that a marked increase and retention of uric acid in the blood may result from the ingestion of purin bases even when no evidence of retention is found on the examination of the urine.

Before diagnostic importance can be attached to this increase in the uric acid of the blood produced by the sweetbread meal in gout, the effect of feeding exogenous purins on the uric acid concentration of the blood in non-gouty individuals must be studied. The low amount of uric acid present in the blood of unselected psychiatric patients on a mixed diet (Folin and Denis, Adler and Ragle) shows that a retention of uric acid in the blood in any considerable amount for twenty-four to forty-eight hours rarely occurs; for these patients on an ordinary diet are eating purin-containing food daily, and they might take as much or more purin in their food during the forty-eight hours preceding the blood analysis as is contained in a single sweetbread meal. If the uric acid derived from this accumulated in the blood, the amount found would be considerably greater than that of individuals on a purin-

free diet. But the average amount of uric acid found by Adler and Ragle in the blood of patients on an ordinary diet was only 0.3 mg. more than that found by McLester in normal individuals on a purin-free diet.

In four non-gouty individuals the uric acid content of the blood has been determined twenty-four to forty-eight hours after feeding a sweetbread meal. The results are summarized in Table III.

TABLE III

	Mgs. of uric acid in 100 gms. of blood.		Mgs. of uric acid in 100 gms. of blood.
McC. Chronic polyarthritis. Purin-free diet	1.7	24 hours after eating 100 gms. of thymus	2.2
R. Multiple recurrent thrombosis; streptococcus isolated from blood. Purin-free diet	1.8	48 hours after eating 300 gms. of thymus	2.3
M. Chronic polyarthritis. Ordinary diet	2.0	24 hours after eating 225 gms. of thymus	1.8
H. Chronic polyarthritis. Ordinary diet	2.9	47 hours after eating 190 gms. of thymus	2.5
Average	2.1	Average	2.2

On comparing the figures given in the two tables it will be seen that prior to the sweetbread meal the average amount of uric acid present in the blood of the gouty and the non-gouty patients was the same. Twenty-four hours to three days after feeding the exogenous purin the average amount of uric acid was 5.1 mgs. in the blood of the gouty, while in the blood of those who did not have gout it was only 2.2 mgs.

Exogenous purins in five gouty patients produced a marked hyperuricemia twenty-four hours to three days after they were fed, while in individuals who did not have gout the uric acid concentration was practically unchanged twenty-four to forty-eight hours after the purin meal.

These observations indicated that the uric acid derived from exogenous purin does not accumulate in the blood unless there is a disturbance in the uric acid metabolism. In one patient, however, who had recurrent iritis, but whose history and physical examination revealed no evidence of gout, the uric acid content of the blood was abnormally high two days after a sweetbread meal. His blood on November 1 after having been on a purin-free diet for two days contained 2.2 mgs. of uric acid. On November 7 he ate 150 grams of sweetbreads. Two days later there was 4.8 mgs. of uric acid in the blood. With the sweetbread meal he took two cocktails. It is possible that the alcohol caused a transitory disturbance of the uric acid metabolism. Pollak has shown that a retarded and

diminished excretion of exogenous purin may occur in chronic alcoholism. No persistent increase of uric acid existed in my patient as the blood examined on March 30 when on a mixed diet contained only 0.8 mg. of uric acid. This is a lower amount than has been found in any case of gout.

The increase in the uric acid content of the blood in gout after feeding a purin meal may not appear for twenty-four hours or more, and an initial fall has been observed in two cases of gout in which the blood was examined four to eleven hours after the sweetbread meal.

TABLE IV

D. N., aged fifty-eight years. Gout. Chronic interstitial nephritis. Purin-free diet begun March 18.

			Diet.	Mgs. of uric acid per 100 gms. of blood.
March	31.	11.30 A.M.	Purin-free	5.8
		12 noon	300 gms. roast beef	
April	1.	11.30 A.M.	Purin-free	4.6
April	2.	11.30 A.M.	Purin-free	4.5
April	3.	11.30 A.M.	Purin-free	6.2
April	4.	11.30 A.M.	Purin-free	2.8

In Case XV of my series, at 10 A.M., two hours before a sweetbread meal, the blood contained 7.2 mgs. of uric acid. At 4 P.M., four hours after taking the exogenous purin, the uric acid had dropped to 5.8 mgs. and the following morning it was 4.9 mgs. at 11 A.M. It seems remarkable that such a drop in the uric acid content of the blood should occur as a result of taking uric acid forming food into the body. The fall in this case within four hours was 1.4 mg. per 100 grams of blood. This is a considerable amount; in fact, it is equal to the average uric acid content found by McLester in fifteen healthy individuals.

This observation on the blood four hours after a purin meal was made recently, and I have not had the opportunity to repeat it on other cases of gout. In one of the first cases studied, Folin and Denis determined for me the uric acid concentration of the blood eleven hours after feeding a gouty patient, whose diet otherwise was purin-free, 280 grams of haddock roe. Only 2 mgs. of uric acid were found, while at a previous examination 3.1 mgs. were present. Two days after the roe breakfast the amount rose to 5.8 mgs. Although eggs of all kinds and caviar are included by von Noorden[14] in his list of purin-free foods, the output of uric acid in the urine rose 0.13 gram on the day the haddock roe was fed.

In two non-gout cases in which I have examined the blood four to five hours after the sweetbread meal, not only did this drop in the uric acid not occur, but there was a distinct increase in the amount of uric acid.

TABLE V

			Mgs. of uric acid in 100 gms. of blood.
F.	Chronic primary arthritis. Purin-free diet.		
	March 9.	11 A.M.	3.0
		12 noon 300 gms. sweetbreads	
		5 P.M.	3.7
McC.	Chronic polyarthritis. Purin-free diet.		
	February 23		2.0
	March 2.	Four hours after eating 225 gms. of sweetbreads	2.7
	March 3		2.0

The blood of a healthy man three hours after taking an ordinary portion of chicken contained 3.9 mgs. of uric acid. Ten days later only 1.3 mgs. was present.

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FOUR CASES OF HEMATOMYELIA: WITH A BRIEF DISCUSSION OF THE ETIOLOGY.[1]

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Hematomyelia, or spinal hemorrhage, is a sufficiently unusual condition to justify the report of cases from a purely clinical aspect and at the same time so much variation of opinion appears to exist as to the probable causation of spinal apoplexy that additional data in regard to this aspect of the problem is definitely valuable.

It was originally designed to report the following four typical instances of hematomyelia with complete microscopic studies of the tissues, and for this purpose the spinal cords were carefully segmented and fixed. Through an unfortunate occurrence the entire collection of tissues was lost and with it the notes detailing the gross appearance of each segment. For this reason it is now only possible to discuss these cases from their clinical and etiological stand-points, but these appear to be of sufficient interest to justify the writer in presenting them.

Case I.—Pilot, aged forty-six years. Had measles when young; malaria off and on for fifteen years. Gonorrhea sixteen, and syphilis twenty years ago.

Spasmodic drinker of beer, whisky, or anything convenient, sometimes drunk every other day. Chews and smokes. Has been always pretty well, save for several minor accidents.

Present Illness. Drank heavily all day, slept very well that night. Went into the saloon the next morning for a bracer. While seated in the rear room he suddenly lost himself and did not rouse until he waked in the alcoholic wards of Bellevue Hospital. Total motor and sensory paralysis below the arms, incontinence of urine and feces. Marked and increasing priapism. Paralysis ascended quite rapidly to arms.

Temperature fluctuated irregularly from 96° to 104.° Pulse rate also varied greatly, not corresponding with temperature curve but ranging from 56 to 120. Respiration entirely diaphragmatic, from 12 to 26, without reference to temperature or pulse. Pulmonary and cardiac status practically normal.

Complete loss of sensation, of temperature, pain, and touch, with complete motor paralysis below level of third dorsal nerves. Patellar, cremasteric, abdominal, and wrist reflexes entirely lost. Incontinence of feces and retention of urine.

After a few days there was some regain of sensation and power in the arms and shoulders. Mentally he became perfectly clear.

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Patient finally sank into a comatose condition and died twenty-three days after the hemorrhage.

Autopsied by permission and on the assurance that only the spinal cord would be examined. A large terminal acute and an old hemorrhage was found involving the cervical and lower dorsal segments. The hemorrhage had followed down the ventricle of the cord, infiltrating out thence into the gray matter. The columns seemed to be free from the lesion. Spinal vessels sclerosed.

CASE II.—J. C., salesman, aged sixty-seven years. Had "bilious" and typhoid fevers in 1865. One attack of gonorrhea. Syphilis denied. Two heat prostrations. Has drunk very moderately. Good and regular habits.

While driving his horse on the speedway he became suddenly dizzy, turned his cart, and collided with another vehicle. Was thrown out, landing on shoulders and head. He remained unconscious for about five minutes during which he was carried to the subway and was met by an ambulance.

Examination showed no voluntary motion below the shoulders. All reflexes below the nipple line were absent. Sensation markedly decreased above this zone. Touch perception present but markedly dulled along the ulnar distribution on both arms. Sensation of heat and cold lost. The paralysis is perfectly symmetrical. There is a small contusion over the sacrum but none elsewhere.

Respiration is entirely diaphragmatic; thorax does not move at all. Forced respiration extends to sternocleido and scaleni muscles. Temperature, 98.4°; pulse, 80; respiration, 24. Very marked continuous priapism.

On the second day the patient developed first a posterior congestion of the base of both lungs succeeded by pneumonic consolidation. Urine and feces incontinent. The mentality became entirely normal; the priapism disappeared.

Seven days after onset the lung status had nearly cleared, but the slight contusions and abrasions of the skin failed to heal, and showed signs of trophic ulceration. Slight movement of the chest muscles became then apparent and the movements of the upper extremities became more improved and better correlated. Slight reflex, after pricking the plantar surfaces of the feet, appeared. Bowels less incontinent. Chest clearing.

Apparent improvement continued until nine days after onset, when quite suddenly the patient became very cyanotic and unconscious. Pulse slow and very feeble; pupils contracted; deviation of left eye; Cheyne-Stokes respiration; complete relaxation of muscles of the extremities; early death.

The autopsy was performed by permission a few hours after death.

The muscles of the paralyzed extremities showed the early evidences of atrophy. Except for the contusions mentioned, there was no evidences of traumatism, no fractures or evidences of

intradural hemorrhage. The arteries and veins of the spinal arachnoid showed some congestion, especially in the upper cervical regions. They were moderately sclerosed.

There was a moderate general softening and a dilated ventricle from the medulla to the sixth cervical segment. Here the gray matter was soft and hemorrhagic and the dilated ventricle was filled with a bloody, grayish, pasty material. The seventh segment showed complete blood infiltration of the gray matter. In the eighth segment the hemorrhage was most marked and had a fresh appearance, especially in the posterior horns. In the first dorsal segment the hemorrhagic softening was very marked in the horns, mostly in the posterior, but in the lower half of the segment it was chiefly confined to the left crescent of the gray matter. In the second dorsal segment the softening was entirely confined to the left crescent, more in the posterior horn, but becoming less and less in the lower levels of the segment. The third dorsal segment showed the same changes in lesser degree, but with general congestion of the bloodvessels.

From this level down to the seventh dorsal there was very little disease, but here the ventricle and its adjacent tissue showed a hemorrhagic softening. The eighth segment showed a simple dilated ventricle without hemorrhage. Blood again appeared in the ventricle at the level of the tenth dorsal segment with the usual extravasation outward. A small psammoma was found attached to the posterior root, on right side, just as it was given off from the cord.

There was a small hemorrhagic area in the left posterior horn of the second lumbar segment; another such area was found located near the ventricle. The third lumbar segment showed a very similar condition. The same was found in the fourth lumbar segment, but the sacral levels showed no changes aside from a general congestion. The cauda showed no gross disease.

The brain showed practically nothing except for isolated patches of slight arachnoid thickening and congested and sclerosed bloodvessels. No hemorrhagic foci were found on gross examination. The arteriosclerosis, which is evidently of long standing, showed moderate calcareous changes.

The basal ganglia showed nothing, and careful sectioning of the pons, cerebellum, and medulla failed to demonstrate any gross abnormalities.

Examination of the general viscera was limited by the terms under which the autopsy was obtained. In so far as studied they showed no lesions of importance except a patchy, pneumonic consolidation, apparently resolving and a chronic interstitial with an acute parenchymatous nephritis. The general bloodvessels showed extensive sclerosis.

CASE III.—A marble cutter, married, aged forty years. Had measles when a child. Fourteen years ago had a gonorrhea. Denies lues.

Five weeks ago had an attack of vertigo which lasted about one week. Nine days ago, while at South Beach, the patient went to stool; being constipated he strained very hard. When he attempted to get up he found that he had lost control of his legs. He had burning pains from the thighs down until three days ago, since which he has experienced shooting pains but twice. His bowels have not moved, and he has to be catheterized. Patient has recently been working in a damp house; to this he attributes his trouble. He has been an inveterate user of tobacco, and has been moderately alcoholic.

He is well nourished, tongue slightly coated, appetite good, bowels constipated. Physical examination of the chest is negative. There is loss of sensation and motion below both knees. Imperfect sensation (heat, touch, pain) of lower one-third of thighs, scrotum, and arms. Cremastic and patellar reflexes, also ankle clonus, absent. Muscles of calves flabby; no priapism at present. Temperature, 98°; pulse, 90; respiration, 24. Mental status entirely normal.

Patient was put to bed, and in addition to general treatment was given daily massage of the paralyzed extremities. At the end of eight days he was moving the legs slightly, but he had developed a trophic ulcer over the sacrum. Sensation was greatly disturbed, but present in some degree even in the legs; distribution did not seem to be constant. Constipation was still very marked and drastic measures were required to induce movements. Cystitis no better.

Thirty-four days after admission he had regained control of the sphincters in large part, but atrophy of the involved extremities was steadily increasing. Cystitis and the bed-sore became progressively worse. He sank into an apparently septic condition, and died forty-one days after admission, fifty days after the acute onset.

The autopsy was performed eighteen hours after death.

Body extremely emaciated. Extreme atrophy of both legs, especially of the anterior tibial groups. No atrophy of the muscles of the upper extremities or of the thorax or abdomen.

The heart showed brown atrophy; the aorta marked endarteritis, but without calcification. Aortic and mitral segments thickened. The large vessels of the abdomen showed moderate endarteritis. Lungs showed emphysema and cavitation in the apices, apparently tuberculous, but no longer active. The liver was fatty. The kidneys showed marked chronic interstitial and fatty, with parenchymatous changes. The renal arteries showed marked endarteritis. The bladder showed ulcerative cystitis.

The second to the sixth inclusive posterior spinal processes were bifid. The vessels of the spinal canal showed extreme congestion,

especially in lower dorsal and lumbar regions. They showed moderate sclerosis. The spinal dura was normal. The first evidence of spinal disease was found at the first dorsal level, manifested by a small area of softening in the left anterior horn. At the level of the fifth dorsal segment the entire gray matter was soft and infiltrated with blood. In the mid-dorsal region the anterior horns appeared to be almost universally softened. In the lower lumbar region the softening had so generally involved all structures as to convert it into an unrecognizable mass.

The direct cause of death was sepsis originating from a large trophic ulcer over the sacrum or from the cystitis.

Case IV.—The patient entered the fourth medical service of Bellevue Hospital unable to give any personal history, and the few details obtained were given by her neighbors.

She was twenty-five years old, supposed to be in good health, and no previous illnesses were known of. She was known among her neighbors as a hard drinker and as of liberal morals. Two days previous to her entrance to the hospital she complained of some headache. On the succeeding day she still suffered, and during the morning drank a quart of whisky. In the afternoon she felt considerably better, but at about 6 P.M., while at stool, she noticed that her feet and hands were becoming numb. She was taken to the hospital on the next day. Absolute anesthesia and paralysis of the lower extremities, abdomen, and, to a lesser degree, of the thorax also, together with slight involvement of the upper extremities. The paralysis and anesthesia rapidly extended upward, and she died before her physical examination had been completed.

The autopsy was performed early the next day, the body having meantime been preserved by efficient cold storage. The external examination of the body revealed nothing except that the pupils were irregularly dilated. The condition of the body indicated involuntary evacuations of feces and urine.

Examination of the spinal canal was only permitted. A large amount of clear colorless cerebrospinal fluid was found, and the vessels of the channel, including those of the spinal dura, were found much congested and considerably sclerosed.

Gross examination showed involvement of the spinal gray matter alone. It was found to be the seat of an acute hemorrhage, softening extending from the cervical levels downward. Apparently the hemorrhage had progressed along, and mostly, if not entirely, through the medium of the ventricle of the spinal cord.

One factor which all of these instances possess in common is that in each, definite disease of the spinal bloodvessels was present. In Cases I and IV syphilis is thus, in all probability, the chief determining factor, and in Case II age is apparently of most definite bearing, though this example also presents the only instance of a possible traumatic factor. Case III represents as the most likely

agent concerned in the production of arterial disease the excessive use of tobacco and alcoholism, which is also a factor in Cases I and IV.

These facts are in direct contraversion to the commonly accepted text-book statement. Thus Church and Peterson state that the changes in the arterial coats are of lesser importance in spinal hemorrhage, and E. Farquhar Buzzard, in Osler's *System* (vol. vii, p. 274), makes the statement that sclerotic changes in the vessels do not appear to very generally determine the lesion. The author is impressed from the statements made by most authors that cases have not been adequately investigated as to this possibility, which is of acknowledged importance in every other type of hemorrhage. It would appear to the writer that spinal hemorrhage in this characteristic in no way differs from hemorrhage elsewhere, and that it is especially similar to brain hemorrhage.

The statement is made by some authors that spinal hemorrhage customarily takes place in a previously existing area of softening. Though it is impossible to absolutely exclude this possibility, at least it seems highly improbable, for in the cases thus reported any lesion of sufficient size to favor such a condition could not long exist in so limited and vital a territory as the spinal cord without producing symptoms of an obvious character. Such signs are entirely wanting in these cases. Eichorst, in 1874, recognized that central hemorrhage might take place in previously normal cords, and in all probability this is the rule and not the exception.

As to the immediate determining factor, Buzzard states the most frequent to be trauma or strain, and Church and Peterson seem impressed with the idea that arterial pressure and direct cardiac impulse which play so important a role in brain hemorrhage are absent or unimportant matters in spinal hemorrhage. The writer's impressions from a study of the literature of the subject and from these 4 cases is that precisely similar factors are at work here as in cerebral hemorrhage, but obviously under conditions varying from those dominant in cerebral hemorrhage. Thus, for example, we find cerebral hemorrhage occurring most frequently in conditions of mental strain, and in all except Case II of this group a definite factor of primary spinal stress was present. Straining at stool was apparently the immediate cause in two of my cases. Oppenheim cites a case occurring during the manual of arms drill. Gowers mentions a case occurring after excessive coitus, and so on.

Traumatism is mentioned by most authors as an important factor in the cause of spinal hemorrhage. One should exclude in this discussion those instances in which actual crushing of the cord occurs, since the lesion in true hematomyelia is one of gray matter hemorrhage only and is quite distinct from that which might occur in direct spinal injuries. In only one of these four instances is a possible traumatic factor concerned, that is in Case II. It must,

however, be noted that no evidence of direct spinal injury was found postmortem in even this instance, and it is possible that the hemorrhage caused the fall, resulting in the accident, and not *vice versa*.

As is always the case in hematomyelia, the blood extravasation has extended along and about the spinal ventricle, and in no instance has extended out into the white matter. This is doubtless due, as all students of the subject have conceded, to purely mechanical factors.

In conclusion, as a result of the study of these instances, one is impelled to the idea that contrary to the prevailing view, arterial changes as a predisposing factor are present in hematomyelia, and that the dominant agent in the immediate determination of the hemorrhage is that of strain, involving spinal activity or tension.

THE USE OF THE DUODENAL CATHETER IN DIAGNOSIS.[1]

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After the first attempts to catheterize the duodenum, many years ago, by Hemmeter[2] and Kuhn,[3] this procedure was looked upon purely as a scientific curiosity, principally because of the cumbersome instruments used, until 1910, when Einhorn[4] and Gross[5] each devised a simple rubber tube, with a metal tip, which they managed to get past the pylorus with more or less ease. After the introduction of these improved instruments it was found by Einhorn[6] that they could be used satisfactorily in the treatment of several diseases, notably gastric and duodenal ulcers, gastritis, and pylorospasm. Einhorn and others have since found it of value, also, in the treatment of certain other troubles of the gastro-intestinal tract, such as the toxic vomiting of pregnancy,[7] duodenitis, etc. Recently, moreover, Einhorn[8] reports favorable results in cases

[1] From the Medical Department of the University of Texas School of Medicine.
[2] Arch. f. Verdauungskr., Band ii.
[3] Ibid., Band iii.
[4] Jour. Amer. Med. Assoc., 1910; Berl. klin. Woch., 1910, Nos. 12 and 34; Arch. f. Verdauungskr., Band xviii; Ibid., Band xix.
[5] Münch. med. Woch., 1910; Wien. klin. Woch., 1910; Arch. f. Verdauungskr., 1914, xx, 338.
[6] Loc. cit.
[7] Morgan, Amer. Jour. Med. Sci., 1914, cxlviii; Carroll, Maryland Med. Jour. 1913, lv, 243; Hess, loc cit; Palefski, Interstate Med. Jour., 1914, xxi, 997; Reuss, Berl. klin. Woch., 1914, li, 1023; Hess, Verhandlunge der Gesell. f. Kinderheilkunde, 1913.
[8] Loc. cit.

of cirrhosis of the liver and cardiac decompensation, where it is desired to give an irritable stomach a complete rest.

Except as a means of treating these diseases, the duodenal tube has been regarded until quite recently as an instrument of comparatively little diagnostic value. It has facilitated the study of the pancreatic secretions, the bile, the flora of the duodenum,[9] etc., but has not been of any great diagnostic importance except, occasionally, in a case of advanced pancreatitis, perhaps, or in complete obstruction of the ampulla of Vater from new growths, gall-stones, etc. (Einhorn, Chase[10]).

Quite recently, however, some rather interesting observations on the use of the duodenal tube in diagnosis have been made. Chase[11] has reported a study of the pancreatic ferments in a number cases, including a few of pancreatitis. Einhorn[12] reported recently some observations of the bile in gall-stone disease, in which he concludes that a turbidity of this fluid is of some significance in diagnosing such conditions. He also believes that the continued absence of any one of the pancreatic ferments is significant in the diagnosis of pancreatitis. Einhorn noted, also, an increased amount of mucus in the duodenum in certain cases of duodenitis, and believes this to be of some value in the diagnosis of that condition. Crohn[13] has recently published a report of several interesting cases of new growths about the head of the pancreas in which the absence of the pancreatic ferments was an important factor in the diagnosis. Bondi and Salomon,[14] of von Noorden's Clinic, have reported several cases of achylia pancreatica diagnosed by means of this tube, and Bondi[15] has also reported a thorough and complete study of the duodenal contents, both microscopically and chemically, in a great number of conditions. Bondi's observations are of such interest, and bear so closely on the work which we are about to report, that perhaps a few words regarding his findings will not be superfluous. His report is based upon the chemical and microscopic analyses of 200 duodenal contents, coming from 153 different individuals. He concludes, as a result of this experience, that such an analysis is of considerable diagnostic importance in certain diseases. In one case of cholecystitis, for instance, he was able to confirm the diagnosis from the presence of innumerable bile-stained pus cells in the duodenal contents. In one case of acute duodenal ulcer the presence of blood and pus cells gave some rather definite information as the local trouble. In certain systemic diseases, moreover, associated with considerable blood destruction, he was able to demonstrate a decided increase in the urobilin content

[9] McNeal, Arch. Int. Med., 1913, xxi, 178; Hess, Jour. Infect. Dis., 1912, xi, 71.
[10] Einhorn, loc. cit.; Chase, Arch. Int. Med., vol. xii.
[11] Ibid.
[12] Amer. Jour. Med. Sci., 1914, cxlvii, 490.
[13] Ibid., 1914, cxlviii, 839.
[14] Wien. med. Woch., 1913, lxiii 1722.
[15] Arch. f. Verdauungskr., Band xix.

of the bile removed by means of this tube. His results were disappointing in a number of cases of ulcer of the stomach and duodenum, however, the contents being apparently quite normal.

Bearing in mind the above-mentioned researches, and believing that there is still a remarkably fertile field for research along these lines, we feel that the report of certain investigations in which we have been engaged for the past eighteen months would not be out of place.

Our technique in making these examinations has differed rather materially from that ordinarily employed. In the first place we have found that a careful microscopic study of the empty stomach contents, with particular attention paid to the cellular elements, will, in many cases, give definite information as to the condition. This is true, also, of the microscopic examination of the duodenal contents. The recent interesting reports of Loeper and Binet,[16] and of Simon[17] and Chaussade,[18] in France, on this subject, have stimulated our belief in the efficacy of direct microscopic study of the stomach contents materially, and while we believe that these authors are perhaps somewhat optimistic in their conclusions, nevertheless we believe that important information is often overlooked by the neglect of such a study. For this reason we have, since the inception of this work, in our endeavor to obtain the gastric and duodenal secretions in a natural state, and unaffected by any artificial means, carefully avoided the administration of tea, as recommended by Einhorn in the passage of this tube, or of water, etc., as recommended by others. Observing this precaution, and given a perfectly empty stomach, we are able to obtain a pure secretion in practically every case. The results which we have obtained from such a study we shall take up in detail in this paper. We have, moreover, found a modification of the Einhorn tube, the so-called Jutte duodenal tube, to be superior to any other duodenal catheter which we have tried for our purposes. We prefer this tube for two reasons: In the first place the tip is practically of the same diameter as the tube, allowing a more rapid passage of the pylorus. In the second place the tube is provided with a stiff wire, enabling one to pass the tube through even an acutely irritable pharynx with little or no difficulty. The wire can be easily withdrawn as soon as the pharynx is passed. With these two exceptions we pass the tube in the usual manner. Contrary to the opinion of some (Palefski[19]), we believe that the passage of this tube is an extremely simple procedure, and that it can be readily passed in the usual case by any physician of moderate intelligence. We find that a small rubber aspirating bulb facilitates the removal of the secretions considerably.

[16] Arch. d. mal. de l'app. digest., 1914, viii, 181.
[17] Press Méd., 1914, xxii, 265.
[18] Rev. de Méd., 1914, No. 6.
[19] Loc. cit.

Our examinations of the contents removed have consisted in the following steps:

1. Gross appearance: color, amount, mucus, blood, etc.
2. Microscopic: pus and blood cells, gastric epithelial cells, amount of mucus, bacteria. In the duodenal contents all bile-stained cells should be carefully studied.
3. Chemical: free HCl, total acidity, lactic acid, Wolff-Junghan's test for dissolved albumin, pancreatic ferments.

Perhaps it would be well to state that two requisites must be observed before one draws any conclusions from such a study as that above outlined. One must, in the first place, be perfectly familiar with the microscopic appearance of the contents from the normal empty stomach and duodenum. This is more easily said than done, and can be accomplished only after the study of a number of normal cases. The chief difficulty with which one has to contend at first is that of differentiating in the gastric contents the true gastric epithelial cells from pus cells, alveolar cells from the lungs, epithelial cells from the mouth, pharynx, and esophagus; and, in the duodenal contents, one must, of course, recognize the cells which have come from the stomach. We are satisfied, however, that with a sufficient amount of experience the important cells in both gastric and duodenal contents can be recognized with little difficulty. The next requisite which must be observed is the prompt examination of the secretions as soon as they are removed, and before the important cells have lost their characteristic appearance from digestion. The examination is best made in the fresh state, using first low and then high power, in the same manner as one ordinarily examines urine for casts.

Our findings with the above technique have been encouraging. In some 25 normal cases we have found rather constant pictures. The free HCl ranged from 0 to 30, the total acidity from a trace to 30, the total acidity usually varying only a few points from the free HCl reading. We have found a fairly constant amount of mucus in the normal stomach contents, usually consisting of white strands floating in the secretion, and containing always numerous polymorphonuclear cells. It must be borne in mind that the appearance of many leukocytes enclosed in this mucus is normal. It is only those leukocytes which are floating free in the secretion which are of significance. A few oval or cylindrical gastric epithelial cells are also often found, but such cells are never very numerous. Our observations in this regard have agreed with those of Chaussade and of Loeper and Binet, to whose excellent studies of the cytology of the empty stomach in normal and morbid conditions the reader is referred for further details.[20] As for the Wolff-Junghan's[21] test

[20] Chaussade, loc. cit.

[21] Berl. klin. Woch., 1911, Med. Klin., 1912; Smithies, Amer. Jour. Med. Sci., 1914, cxlvii, 713; Rolph, Med. Rec., 1913.

of the empty stomach contents under normal conditions, we find that the percentage of dissolved albumin is fairly constant, the ring appearing practically always in either the second or third tube, rarely in the fourth. The duodenal tube passes the pylorus in the great maiority of these cases in from ten to fifteen minutes after its introduction.

The microscopic study of the normal duodenal contents is simple. The fluid is clear, bile-stained, seromucous, and contains few cells except for the partly digested gastric cells, which have already been noted. The Wolff-Junghan's test of this secretion usually gives an albumin ring in the third tube, occasionally in the fourth, but, in our experience, never in the fifth or sixth tube normally. So far as I am aware there are no previous reports as to the application of the Wolf-Jughan's test to the duodenal contents. Brauer[22] has shown that the bile of the normal dog is albumin-free, but that albumin appears in it after the administration of phosphorus, alcohol, etc., in toxic doses, so that, apparently, the presence of albumin in this fluid is a sign of damage to the liver. Unfortunately, however, we have three other albumin-containing secretions to deal with before we can draw any definite conclusions as to the increase of albumin in the duodenal contents. Fortunately we can control the albumin content of the stomach by direct examination, and when there is a material difference between the readings of the gastric and duodenal secretions in this regard, we know that the increase must come either from the bile, from the pancreatic secretion, or from the secretion of the duodenum itself. Only extensive experience will show whether such a test is of material value, but several observations which we have made have at least been interesting to us. The three pancreatic ferments we have found to be present constantly in normal cases.[23]

Our series of studies on pathological conditions of the gastro-intestinal tract consists of observations on some 60 selected cases, which we shall take up in detail. The most common condition studied in our series has been chronic gastritis. We have 12 cases of this condition, in which the findings were fairly constant and were as follows: The secretion is usually obtained from the stomach with some little difficulty, being often tenacious from an excess of mucus. (Occasionally it becomes necessary to inject several hundred centimeters of water, preferably normal saline, before a sufficient amount can be obtained. This is exceptional, however.) There is usually no free HCl. The reaction is apt to be neutral, or, at least, very faintly acid. Occasionally, however, both the free HCl and the total acidity are fairly high. Micro-

[22] Zeit. f. Physiol. Chemie, Band xl.

[23] These tests have been carried out in the usual manner: that of Wohlgemuth for diastase; of Gross for trypsin, and the method described by Bondi, for lipase (loc. cit.)

scopically, one sees numerous well-preserved pus cells floating free of mucus. A few flecks of blood may be observed in the mucus. In the very old chronic cases, gastric epithelial cells are usually very scarce, if not absent. In a few cases, however, they have been more numerous than normal. Considerable difficulty is usually experienced in these conditions, in getting the tip of the duodenal tube past the pylorus, apparently due to a lack of gastric motility. In two of this series it was necessary to leave the tube *in situ* over night before the duodenal contents could be obtained. A typical picture of this condition would therefore be, in our experience, an excess of mucus, causing a thick, tenacious secretion, few cellular elements (except pus cells), and a sluggish motility, with no free HCl and a low total acidity.

The cases of acute and subacute gastritis, which we have studied, of which there were four, have differed from this picture in several respects. In the first place, there was usually a fairly high percentage of free HCl, as well as a higher total acidity. There is not usually so much mucus. In all of our cases the cellular elements were materially increased, especially the gastric epithelial cells, which often appeared in showers, as it were, being numerous in one specimen examined and not so numerous in the next. They were always increased, however. The pylorus was passed with little difficulty in three cases. In the fourth considerable difficulty was experienced. It may be well to state here that our diagnoses, both of the acute and the chronic gastritis, were made from the ordinary clinical and laboratory examinations, and not by means of this study. A fairly large percentage of them were operated upon for other conditions, at which time the diagnosis was confirmed at operation (four cases). We feel, however, that this direct method of study would perhaps bring about a better classification of such conditions.

We have studied three cases of hypersecretion in this series. In all three of our cases there was a continuous watery, highly acid secretion, there being apparently no tendency for the secretion to cease so long as the tube remained in place. The free HCl in these cases varied from 60 to 80. Microscopically the gastric and duodenal contents of two were negative. There was a definite increase of the gastric cellular elements in the third case, which we believed to be a case of gastritis (from this study). One of these cases was demonstrated at operation to have no evident organic cause accounting for the trouble. Laboratory and Roentgen-ray examinations were negative in the other two. All three were strong, robust men. We believe that this method is an ideal one for the study of these cases of hypersecretion.

The study of ulcer of the stomach and duodenum in our cases has been disappointing. In acute, actively bleeding ulcers one can, of course, recognize the red blood cells, which are usually

partially hemolized. We have been able, in one case of suspected ulcer, as judged from the other laboratory tests, to say from the direct study, that it was probably a case of chronic gastritis, which diagnosis was confirmed at operation. With the exception of the bleeding above mentioned, which we have never found in the chronic or subacute cases, there is in our experience no information to be gained from such a study as we have made. We have felt, on one or two occasions, that the presence of a few red blood cells, enclosed in mucous strands, with perhaps more gastric cells than normal, would point to ulcer. In one such case in particular we felt so sure of this that we were willing to make a positive statement to that effect. The case turned out to be, at operation, a carcinoma of the cecum. The gastric cells and red blood cells certainly came from a gastritis, but I may say that the case was typical, clinically, of duodenal ulcer. With one case of syphilitic ulcer of the pylorus, however, we have had better success. In this case the appearance of numerous, free red blood cells, along with innumerable pus cells and cylindrical gastric cells, which were only noted when the tip of the tube had become engaged in the pylorus, led us to state certainly that there was an ulcerative process at the pylorus. This was confirmed at operation, which was done on the suspicion of carcinoma. This case has already been reported.[24]

Our study of a limited series of cases of carcinoma of the stomach, six cases, of which two were operable, has been interesting to us. In the first place, we find, as a rule, a picture at first suggesting a subacute or a chronic gastritis, both from the gross and from the microscopic appearance. As for the finding of cells showing malignant changes (mitoses, etc.), upon which some writers lay such stress,[25] we have been rather unsuccessful,[26] perhaps because we are not sufficiently trained in the proper technique, but certainly we are unable to substantiate their claims as the great value of these cells in diagnosis. We find, however, in addition to the signs of a gastritis in these cases, a rather interesting chemical change. In all of our cases free HCl was entirely absent from the content of the empty stomach, and the total acidity, instead of remaining low, as in chronic gastritis, was in all of our series except one compaartively high, ranging from 25 to 60. Lactic acid was, of course, present in the advanced cases only. Another interesting feature of such a study as this is the comparison of the acidity (free and combined HCl) of the empty stomach to that obtained after an ordinary test meal. This test, a modification of the well-known Glutzinski test, was suggested by Ehrenreich:[27] In normal cases,

[24] McNeil, Jour. Amer. Med. Assoc., January 30, 1915.

[25] Chaussade, loc. cit.; Loeper-Binet, loc. cit.

[26] In two cases, however, we have found cells which were very suspicious of carcinoma cells.

[27] Berl. klin. Woch., 1914, No. 33.

and also in gastric ulcer, the acidity rises after such a test meal. In carcinoma ventriculi, however, it remains practically stationary, or may even be lowered. In chronic gastritis it usually rises slightly, and occasionally the rise is rather marked. Two of our carcinoma cases showed a slight increase in acidity after a test meal, but none showed the material increase which is present normally. The results of the Wolff-Junghan's test, as applied to the contents of the empty stomach, in these cases showed constantly, a rather high albumin content, the readings on the empty contents being about the same as after a test meal. We have found this test either positive or suggestive in all of our series of carcinoma cases, and believe it to be of some value. We believe, however, that the positive test can be foretold in many cases from a microscopic study of the stomach contents; those cases showing many cellular elements, especially, pus cells, often having a high reading. This point deserves further study, however. The passage of the tube through the pylorus will, of course, depend upon the location of the growth. The duodenal contents were normal in these cases.

We have studied only one case of carcinoma of the head of the pancreas. In this case there was obstruction to the ampulla of Vater, and we were able to make the diagnosis from the absence of pancreatic ferments in the duodenal contents and in the stools.

We have had an opportunity to study only one case of chronic pancreatitis, of which we were sure. This case was associated with a pancreatic cyst, and showed a constant diminution in the pancreatic ferments, and usually an absence or only a trace of lipase. These tests were made both on the stools and on the duodenal contents. This case was also interesting clinically, showing a transient glycosuria, periodic attacks of abdominal pains and tenderness, inability to digest excess of fats, etc.

Three cases of achylia pancreatica were studied by means of this tube. All showed clinical signs suggesting the stomach as the seat of trouble rather than the pancreas, but pancreatic ferments were constantly absent from the duodenal contents in all three cases. In all three cases, however, diastase was demonstrated in the stools after the manner described by Brown, so that one might be justified in doubting whether these were really cases of pancreatitis. Such cases are certainly not normal, and undoubtedly call for further study. None of these three went to operation, so that we have no means of knowing the true condition. The stools of all three showed a certain amount of azotorrhea, and in one case this was marked.[28]

Our opportunities to study acute cholecystitis by this method have, unfortunately, been rather limited. Observations have been

[28] Since this was written one of these latter cases has come to operation, which revealed a much hardened and indurated condition at the head of the pancreas. A diagnosis of chronic pancreatitis was made by the surgeon. No other abnormalities were found.

made only on three cases. In one we were able to confirm the observation of Bondi as to the presence of bile-stained pus cells. They were not so numerous, however, as one would expect. In the other two these were not found, but in one, typhoid cholecystitis, in addition to numerous typhoid bacilli, we found numerous bile-stained cells, which we believe to have come from the epithelial linings of either the gall-bladder or some of the gall passages. The third case, a subacute one, showed nothing of note except possibly a few more cellular elements from the biliary tract than one would expect.

In four cases of atrophic cirrhosis of the liver which we have studied by means of this method, we have found several pictures which have interested us considerably. In two cases we have found quite a number of bile-stained, polymorphonuclear cells, associated always with cells which we are accustomed to call "liver cells." These cells are, in our experience, not found under normal conditions in any appreciable number. One or two, in several preparations, may perhaps be noted, but we have never found them numerous except in this condition. They are slightly larger than the normal polymorphonuclear leukocyte, are always rather deeply bile-stained, as contrasted with the cells coming from the stomach and elsewhere, have a granular, refractile protoplasm, and are round or oval in shape. There is a single, small central nucleus. Occasionally a group of these cells will be found arranged in the form of a cast. In all four of our cases such cells were fairly numerous. We were also greatly interested in the albumin content of the duodenal contents in these cases for the reason previously mentioned. Three of these cases failed to show any albumin increase by the Wolff-Junghan's test, but one case, in an early stage, showed a marked increase over the normal. An operation had been preformed on this case and a typical hob-nailed liver had been found unexpectedly. This case also showed numerous bile-stained cells, such as we have described, although no pus cells were seen.

One case showing a large tender liver, and who had also a strongly positive Wassermann reaction, showed a marked increase of albumin in the duodenal contents, although the albumin content of the stomach was normal. This case, however, showed nothing abnormal in the duodenal contents microscopically. There is also one other peculiarity about these cases which we have frequently noted, which was found likewise in our cases of gall-bladder disease: This is the presence of bile in the gastric contents removed from the empty stomach. Einhorn[29] has found this phenomenon to be present in several cases of gastroptosis. We have found it so far only in these cases above mentioned, and in one case which we believed to be duodenitis. The presence of a turbid bile, which Einhorn mentions,

[29] Amer. Jour. Med. Sci., cxlviii, 490.

has also been noted in several of these cases, in two cases of cholecystitis and in two cases of cirrhosis. We have also found the bile turbid in several other cases, however, which have been demonstrated not to have had any gall-bladder or hepatic trouble. Three cases of chronic passive congestion of the liver have given negative results from such a study with the duodenal tube.

There is one other condition which is often mentioned, but which is seldom described, in which a study by means of this tube is of interest. This is the so-called duodenitis. Three cases which we have studied in this series have, we believe, been suffering from this trouble. All complained of pain in the right upper abdomen, suggesting in every case gall-bladder trouble. All were men, and all were past middle age. The duodenal contents in each of these cases showed a considerable amount of stringy mucus, numerous gram-negative, motile bacilli, occurring usually in strings, and numerous cocci. These bacteria were in all three cases the most prominent picture in the microscopic field. In all of these cases, also, there seemed to be more leukocytes in the duodenal contents than were found in the gastric contents, although this point may be difficult to determine, since it is merely relative. Two of these cases went to operation. Neither showed any trouble in the abdomen which could account for the symptoms of which they complained.

We have studied four cases of typhoid fever by means of this tube, three of whom were convalescent, in the hopes of discovering the presence of typhoid bacilli in the bile. This we have been able to do in three cases. We would therefore suggest, as Hess[30] and McNeal[31] have already done, that we have in this tube a valuable means of detecting typhoid carriers.

Finally, as a result of this work, which is, unfortunately, limited, but which we hope to continue, we believe that we are justified in drawing the following conclusions:

1. The direct method of study of the pure gastric and duodenal contents is of value in diagnosing certain conditions of the gastro-intestinal tract, *i. e.*, acute and chronic gastritis, carcinoma ventriculi, acute ulcerations, pancreatitis, duodenitis, continuous hypersecretion, etc.

2. We feel that a further study of the hepatic and biliary diseases, along the lines which we have mentioned, would be of great interest, and we feel that, at least in certain cases of such disturbance, such studies might be of great value.

3. The absence of pancreatic ferments in the duodenal contents is a significant feature of obstruction to the pancreatic duct, and is especially valuable when associated with a marked diminution of diastase and trypsin in the stools.

[30] Loc. cit.

[31] Loc. cit.

4. In the duodenal tube we have the only means of studying a disturbance or inflammation of the duodenum itself.

5. The tube is of value in detecting typhoid carriers.

We wish to express our thanks to Dr. R. W. Knox, of the Southern Pacific Hospital, Houston, on whose service many of these cases were observed, and to Professor M. L. Graves, of the University of Texas, for assistance and encouragement in this work, on whose service the remainder of the cases herein reported were observed.

SYNCOPE.

By Lovell Langstroth, M.D.,
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Loss of consciousness is directly due to some poorly understood state of the nerve elements of the brain following a change in their relation to their blood supply. It may be thought of possibly as a widespread retraction of cortical dendrites interrupting their connections with all lower centres. It is not due to diminished nutrition of the nerve elements, because while there is enough extravascular plasma in the brain to supply the nerve cells for a not inconsiderable period of time, in the fatal syncope of aortic regurgitation, loss of consciousness and cardiac failure are almost synchronous. More probably it is due to a sudden diminution of blood-pressure within the skull and thus indirectly to a diminution in the blood supply of the brain.[1]

That cerebral anemia will cause unconsciousness has been quite definitely proved experimentally. Kussmaul and Tenner[2] compressed the carotids in a number of male adults and got dilatation of the pupils, slow, deep, and sighing respiration, dizziness and unconsciousness. Leonard Hill[3] produced unilateral convulsions by compression of a single carotid in man; and animals in which he ligated several or all of the cerebral arteries regularly developed convulsions.

The most prominent features of ordinary syncope are due to the action of the heart. The pallor of the face undoubtedly corresponds to anemia of the brain. The patient feels a sense of increasing feebleness, and is often unduly conscious of the action of the heart.

[1] Sir William R. Gowers, A Lecture on Faints and Fainting, Lancet, 1907, vol. i, 565.

[2] Nature and Origin of Epileptic Convulsions Which Follow Profuse Hemorrhage, New Sydenham Society, 1859, n.s., 95, p. 28.

[3] Cerebral Anemia, Philosophic Transactions of the Royal Society, 1900, B vol. cxciii.

There is often nausea and a sense of prickling of the skin of the face.[4] Sometimes he falls sharply to the ground, though often sufficiently warned by his rapidly increasing weakness to seek the recumbent position. The sight may suffer without loss of consciousness.[5] During the attack the respiration is detected with difficulty and the radial pulse or heart contractions may be imperceptible.[6] The loss and return of consciousness is usually slow, and when regained there is always a correct perception of surroundings.[7]

Syncope frequently occurs in people with normal hearts, and is then indirectly due to various emotions which are induced by impressions usually received through the special senses. Thus certain odors, the sight of blood, an unusual, unexpected, and sudden noise, the touching of some unrecognized and unusual object in a familiar spot in the dark or great fear or sorrow may cause syncope. This emotional fainting is due to inhibition of the nervous system. The constant stream of afferent stimuli to the brain is suddenly neutralized by one all-powerful one with consequent sudden relaxation of muscular tone, collapse of the body, paralysis of the vasomotor system, collection of blood in one set of vessels (the splanchnics), marked diminution in the strength of the contraction of the heart, cerebral anemia, and loss of consciousness.[8] It is not known whether in syncope the heart stops or the contractions become very much weakened[9] or whether its failure is due to diminished blood in its arteries or in its cavities or to diminished blood in the medulla with consequent pneumogastric stoppage.[10] The fact that the sounds are inaudible and the pulse not felt would speak for the latter, though possibly due to extreme feebleness of the contraction.

Mechanical factors play their part in causing a sudden collection of blood in one set of vessels and syncope is not uncommon after withdrawal of peritoneal collections, violent purging, enemata, and paracentesis of the thorax for effusions into the pleural cavity. The release of external pressure apparently causes a sudden paralysis of the walls of the vessels, and if the affected area is large, as is the case with the splanchnics and pulmonaries, enough blood is withdrawn from the general circulation to cause cardiac failure. A similar explanation applies to the syncope of patients who have long been in the recumbent position and are too suddenly raised to the sitting position, but in this case it is the loss of tone of the abdominal muscle that is at fault. Entrance into a warm room from the cold air may cause syncope by sudden withdrawal of blood to the surface of the body.[11] Stooping increases the amount of blood in the head but may sometimes cause momentary unconsciousness.[12]

[4] Gowers, loc. cit.
[5] Ibid.
[6] Allbutt, System of Medicine, vol. vi, p. 516.
[7] Gowers, loc. cit.
[8] Leonard Hill, Further Advances in Physiology, 1909.
[9] Allbutt, loc. cit.
[10] Gowers, loc. cit.
[11] Lewis, loc. cit.
[12] Gowers, loc. cit.

The vagus is undoubtedly concerned in the causation of certain syncopal attacks. Thus the syncope due to agonizing pain probably occurs through vagus stoppage of the heart rather than through a sudden loss of splanchnic tone, and is more likely to be fatal.[13] Thanhoffer[14] took tracings from students who made pressure on their own vagi. In one case he observed standstill of the heart for over one minute and unconsciousness supervened. Mackenzie[15] reported a case in which there was complete standstill of the heart for four to five seconds, often accompanied by syncope. Neuberger and Edinger[16] reported the case of a patient who had faints while at stool, with a slow pulse. At autopsy there was almost complete atrophy of the right half of the cerebellum and a varicose dilatation of the ependymal vessels in the medulla. The rise in blood-pressure while straining at stool probably caused a compression of the medulla near the nucleus of the vagus.

Syncope is frequent in diseases of the heart and vessels. It is well known and may end fatally in fatty degeneration of the heart.[17] In stenocardiac attacks it may take the place of pain. Spasm of the facial muscles with which it is combined allows us to conclude that an active process is going on in the vessels of the cortex as well as in the coronary arteries.[18] In aortic disease it is common. Here the minimal pressure may be quite low, and when the heart is slow and the ventricle weak an extrasystole may cause a dropped beat and abnormal emptying of the arteries.[19] Some of the short attacks of unconsciousness in cerebral arteriosclerosis may be attributed to extrasystoles which are weak in themselves and followed by a slight pause so that the brain is momentarily deprived of blood. This would not occur if the arteries were soft. These short attacks are to be differentiated from ordinary syncope by their abrupt onset and offset and their short duration.[20] Extrasystoles themselves may be the cause of cerebral anemia and syncope. When of the ventricular type they are often so weak as not to overcome the aortic pressure so that the semilunar valves remain closed. A compensatory pause follows, and when such extrasystoles follow every second sinus beat, as not infrequently occurs, the pulse rate becomes only half that of the sinus. With a slow sinus rhythm cerebral anemia and syncope may occur. Paroxysmal tachycardia and paroxysmal fibrillation of the auricles may cause syncope from

[13] Allbutt, loc. cit.

[14] Thanhoffer, Die beiderseitige mechanische Reizung des Nv. vagus beim Menschen, Centralbl. d. med. Wissen., 1875, xiii, 403.

[15] Diseases of the Heart, 1908, p. 345.

[16] Einseitiger fast totaler Mangel des Cerebellums. Varix oblongatæ. Herztod durch Accessoriusreizung, Berl. klin. Wchnshft., 1898, xxxv, 69.

[17] Osler's Modern Medicine, 1907, iv, 220.

[18] Max Herz, Die Herzkrankheiten, p. 191.

[19] Osler's Modern Medicine, 1907, iv, 220.

[20] Herz, loc. cit.

cerebral anemia. The sinus rate itself may be as slow as twenty-five to forty, and such a patient may have syncopal seizures.[21] In congenital cyanosis syncope is not uncommon. Dyspnea is usually a marked feature and frequently culminates in convulsive seizure. A paroxysmal congenital cyanosis has been described by Variot and Sebelleau, in which convulsive seizures with dyspnea and extreme cyanosis occur in patients who at other times are quite free from the latter.[22] Syncope and even convulsions are not uncommon in aneurysm of the arch of the aorta, and have been mistaken for epileptic attacks.

Adams-Stokes syndrome is characterized by syncopal or epileptiform attacks, with a slow pulse, and is due in a large percentage of cases to heart block. The attacks may occcur in the transition period from incomplete to complete block. At this time impulses entirely cease reaching the ventricle, and a considerable period of time elapses before it starts on a rhythm of its own. In this period no blood reaches the brain, and syncope or epileptiform attacks occur. When block is complete and the idioventricular rhythm established, cerebral anemia may occur from some increased demand on the ventricle. In cases where the conductivity is somewhat diminished, sudden stimulation of the vagus centre may cause the heretofore incomplete block to become complete, with consequent cerebral anemia, until the vagus effect stops or the idioventricular rhythm is established.[23] Syncopal attacks in heart block are marked by pallor, disappearance of the pulse at the wrist, unconsciousness, spasmodic twitching of the muscles of the face, and general convulsions,[24] depending on the length of time during which the ventricle does not contract. In the severest attacks there is squint or conjugate deviation of the eyes, wide pupils, noisy respiration, and frothing at the mouth.[25] The relation between the period of ventricular stoppage and the signs of the resulting cerebral anemia are fairly definite. If it lasts two to two and a half seconds there is little or no disturbance. Thus in simple extrasystole the ventricular pause would not be long enough to cause syncope without the addition of some other factor as cerebral arteriosclerosis or muscular insufficiency of the ventricle. When the ventricle stops for fifteen to twenty seconds, epileptiform convulsions begin and a pause of ninety to one hundred and twenty seconds is rarely followed by recovery.[26]

The stupor and drowsiness seen toward the end in cardiac failure bear only a slight relation to syncope. There is probably some

[21] Lewis, The Mechanism of the Heart Beat, p. 265.
[22] Osler's Modern Medicine, 1907, iv, 325.
[23] Hirschfelder, loc. cit., p. 561.
[24] Osler's Modern Medicine, 1907, iv, 220.
[25] Ibid.
[26] Thomas Lewis, loc. cit., p. 266.

cerebral anemia from failure of the left ventricle to properly fill the arterial system, but there is also a chronic poisoning with carbon dioxide.[27]

True syncope is to be differentiated from minor epilepsy, which it may much resemble. Indeed, strong evidence has been offered to show that repeated cardiac syncope has a disposing influence to epilepsy. This suggests that the state of the nerve elements concerned in loss of consciousness may from frequent inductions show a tendency to spontaneous development.[28]

In cardiac syncope the loss and return of consciousness is more gradual than in epilepsy, and the beginning of the attack is marked by pallor, which never occurs in petit mal. Pallor may follow loss of consciousness in epilepsy, but usually there is no change in the color of the face. There is no disorientation on return of consciousness after syncope, the patient immediately recognizing his surroundings. Differentiation is sometimes made difficult by the fact that although external influences are usually the cause of syncope, epileptic attacks may also be brought on by them. In epilepsy the aura may be cardiac. Even sudden change of position and stooping have been known to bring on epileptic attacks as well as cardiac syncope.[29]

[27] Osler's Modern Medicine, 1907, iv, 220.
[28] Gowers, loc. cit.
[29] Ibid.

REVIEWS

Die Thierischen Parasiten des Menschen. By Dr. Max Braun, O. O. Professor der Zoölogie und vergl. Anatomie, Direktor des Zoölogisch. Museums der Universität Konigsberg I.Pr., Geh. Regierungsrat, und Dr. Otto Seifert, A. O. Professor f. Rhino-Laryngologie, Vorstand der Poliklinik f. Nasen- und Kehlkopfkranke der Universität Würsburg. Part I, Naturgeschichte der Thierischen Parasiten des Menschen. Dr. Max Braun. Pp. 559; 407 illustrations. Würzburg: Von Curt Kabitzsch, 1915.

The present work is to be of a monumental character, and like all works originating from the present source, every detail is carefully and completely worked out, and therefore it is a pleasure and benefit to read and study. The volume is so profusely illustrated that almost every other page contains one or more drawings, diagrams, or photographs to illuminate the excellent text. The subject is introduced by a general discussion of parasites and parasitism. The author views the subject "the animal parasites of man" under the following main headings: Protozoa; plathelminthes; nematodes; acanthocephali; gordiacei; hirudinei; arthropoda. Protozoa are divided into a large number of headings, which are reviewed under the general classification of rhizopoda, and includes the various entameba, ameba, and parameba; flagellata; onidosporidia; sporozoa; and infusoria. Plathelminthes are divided into the main headings of trematodes and cestodes. The arthropoda group is divided into two main parts, arachnoidea and insecta. All of the various animal parasites are described, including not only those that attack the various internal organs and structures, but also those that crawl on the surface of the skin and others that migrate in the integument. There is a striking difference in the size of the various animal parasites if one considers those which are microscopic; for instance, the gastrophilus larva, which is pin-point in size, and the guinea worm (dracunculus), which may be over thirty inches in length. One of the most valuable features of the volume is the complete bibliography; ninety-five pages are devoted to all of the literature extant on the subject of animal parasites. It gives the reviewer pleasure to recommend this admirable book to anyone interested in this rapidly-growing and until recently, comparatively little-touched field of medicine. F. C. K.

THE PRACTITIONER'S VISITING LIST FOR 1916. Four styles, weekly, monthly perpetual, sixty-patient. Philadelphia and New York: Lea & Febiger.

WE again welcome the appearance of this useful volume. Like its predecessors, the *Practitioner's Visiting List for 1916* contains much practical information of the sort that physicians constantly need, arranged in a way to make it quickly and easily accessible. Such data as the ligation of arteries, tables of dosage, methods of examining urine, and comparative scales showing the equivalent in the metric system of ordinary weights are measures to be mentioned among the topics touched on. The essential feature of this book is the visiting list, which is admirably adapted to the most exacting needs of the busiest practitioner. G. M. P.

CASE HISTORIES IN DISEASES OF WOMEN, INCLUDING ABNORMALITIES OF PREGNANCY, LABOR, AND THE PUERPERIUM. By CHARLES M. GREEN, A.B., M.D., Professor of Obstetrics and Gynecology in Harvard University; Senior Surgeon for Diseases of Women, Boston City Hospital. Pp. 477; 11 plates, 1 cut, and 25 charts. Boston: W. M. Leonard, 1915.

THE author, a pioneer in the case history method of teaching, presents a systematic review of the pathological processes of the female reproductive organs from infancy to senility. The subject matter is divided into five parts. In each section we find a brief yet comprehensive consideration of the predominant morbid processes peculiar to the period of a woman's life under discussion. These are grouped in each section as Functional Disorders, Malformations and Displacements, Infections, Traumata, and Neoplasms. Following the sectional introduction are the illustrative case histories and appended to each is a short comment on the various features of the case.

Section one reviews the conditions encountered during infancy and childhood. Eight histories serve to make clear the various disorders. The histories are abstracted to include the history of the diseased condition, the diagnosis and prognosis, method of treatment, and the comments.

Section two takes up puberty and adolescence. The disorders of menstruation are considered fully, and among the twenty-two illustrative case histories are typical examples of the various forms of amenorrhea and dysmenorrhea.

Section three deals with the morbid conditions of maturity.

This section comprises over two-thirds of the text and includes the histories of one hundred and thirty-three cases.

References to abnormalities of the reproductive processes are very complete. The author evidently treats the toxemia of pregnancy in a very conservative manner, and is opposed to any local measures in puerperal sepsis. Febrile conditions in the puerperium, aside from sepsis, scarcely mentioned in some text-books, are illustrated by histories and temperature charts. The graphic description of pelvic infections is an interesting part of the introduction to the section. Malignant disease of the pelvic organs receives full attention.

Section four reviews the decline of the sexual life of woman, the climacteric, and the eleven histories detail the most frequently encountered pathology.

Section five, on anility, completing the volume, brings up the occasional atrophic lesion in those whom the author considers "old women."

The book is an interesting one, the histories are instructive, many excellent suggestions in treatment are given, and there is often a pleasantly personal tone to the comments.

The volume will rank high in the Case History Series, and will be of interest and service to anyone whose practice includes the care of women. P. F. W.

EXERCISE IN EDUCATION AND MEDICINE. By R. TAIT MCKENZIE, A.B., M.D., Professor of Physical Education, and Director of the Department, University of Pennsylvania. Second edition; pp. 585; 478 illustrations. Philadelphia and London: W. B. Saunders Company, 1915.

THIS new edition of Dr. McKenzie's well-known work is sure to have an even greater success than at its earlier appearance. More and more attention is yearly being paid to exercise, not only to its value in general, but to the importance of careful and scientific control of its quality and quantity. Exercise can no longer be advised in a vague, indefinite manner: it must be adapted to the individual and fitted to special needs. A faulty prescription for exercise may be as harmful as any therapeutic error, while exercise properly employed may cure certain ills when all other measures fail. The normal child and adult, the scoliotic, the tabetic, and the cardiac can all exercise with benefit, but not in the same manner or amount. If this book contained no more than this information it would appeal to few outside the medical profession. However, it contains much more, and includes in the first part (320 pages) a thorough discussion of the various systems of physical

training employed abroad and detailed descriptions of methods of physical education in schools, colleges, municipal playgrounds, etc. Special chapters are devoted to the physical education of the blind, the deaf-mute, and of mental and moral defectives. Part II covers the subject of exercise in medicine, and describes, almost too conservatively, what can be accomplished by exercise in the treatment of flat-foot, club-foot, visceroptosis, constipation, respiratory diseases, diseases of the circulation, obesity, tic, stammering, chorea, and other conditions. There is no need in going further. The work is all inclusive, well written, and lavishly illustrated. Except for an amusing misprint in a quotation from Solon on the front page, the printer has done his work well. The author, Dr. McKenzie, is at present in England at one of the large training camps, so we may look forward to additional chapters on military training in future editions. O. H. P. P.

MEDICAL ELECTRICITY, ROENTGEN-RAYS, AND RADIUM, WITH A PRACTICAL CHAPTER ON PHOTOTHERAPY. By SINCLAIR TOUSEY. A.M., M.D., Consulting Surgeon to St. Bartholomew's Clinic, New York City. Second edition, thoroughly revised and enlarged, Pp. 1219 798 illustrations, 16 in colors. Philadelphia and London: W. B. Saunders Company, 1915.

THE author is recognized as an authority by those engaged in the practice of electrotherapeutics and roentgenology. Possibly only those who are familiar with these subjects can appreciate the stupendous undertaking represented in the compilation of a book of this kind. Although this is a new edition which is supposed to be thoroughly revised, it must be truthfully stated that the book is not up-to-date in several respects. The subject of roentgenology alone is broadening so rapidly, and ideas and methods are changing so constantly and extensively, that it is almost beyond the power of any one individual to keep a book as comprehensive as this one is supposed to be thoroughly abreast of the times. The roentgenologist can realize this and can make allowances, but the student or beginner may be easily mislead into false impressions. Gastro-intestinal diagnosis is one of the most important branches of roentgenology at the present time, but the author deals with it in a very unsatisfactory and incomplete manner. He states that he is strongly opposed to the use of the fluoroscope in gastro-intestinal diagnosis, whereas this method is now generaly recognized as being absolutely essential for the diagnosis of many conditions of the digestive tract. There is much valuable data concerning roentgen diagnosis and treatment that might well be substituted for much information the book contains that is of comparatively little value.

More than half the space is devoted to the physics and physiological effects of electricity and to electrotherapeutics. A short section deals with phototherapy and another with radium and its applications. A large part covers the subject of roentgen diagnosis and therapy. H. K. P.

A Manual of Surgery. By Francis T. Stewart, M.D., Professor of Clinical Surgery, Jefferson Medical College; Surgeon to the Germantown Hospital; Out-patient Surgeon to the Pennsylvania Hospital, Fourth edition. Pp. 774; 580 illustrations. Philadelphia: P. Blakiston's Son & Company, 1915.

The fact that this work has gone to its fourth edition does more to show its true worth and popularity than any criticism the reviewer may make. This last edition more fully elaborates on the more recent advances in surgery. Bronchoscopy, esophagoscopy, proctoscopy, roentgenography all have been expanded. Transfusion, hemorrhage, spinal puncture, colectomy, hernia, tumors of the hypophysis, and surgery of the lung, liver, stomach, spleen, and breast all have been revised and brought to date as regards their diagnosis and treatment.

New sections on the exclusion of the pylorus, sporotrichosis, surgical purpura, and hand conditions, and transplantation of fat, fascia, bone, and veins have been added.

Many new illustrations have been added and some old ones discarded. One really adverse criticism is that even now the author wastes valuable space with many illustrations that are not appropriate for students and practitioners. The book, however, is an excellent one, and with the exception of a few ideas on fracture treatment, will serve admirably for general use.

E. L. E.

Diabetes Mellitus. By Nellis B. Foster, M.D. Pp. 243. Philadelphia: J. B. Lippincott Company, 1915.

In the first chapter of this volume the author presents in a clear and concise way the principal factors that govern the general metabolism of the animal body. The subsequent three chapters are devoted to a discussion of the role of glucose in the animal body, experimental glucosuria, and the influence of glucose on the metabolism of fats and acidosis. The author then proceeds with a discussion of the pathogenesis, history, etiology, and pathology of human diabetes. The last one hundred pages are devoted to a description of the symptoms, diagnosis, and treatment of the

disease, with a final chapter on the chemical methods of identifying and determining sugar in the urine and blood.

This work is recommended to the practitioner of medicine for two reasons: First, because it will enable him to better understand and manage a disease which he is frequently called upon to treat, and secondly, because it will give him an insight into the perplexities of the problems which so baffle the medical investigator.

A. I. R.

WHEELER'S HAND-BOOK OF MEDICINE. By WILLIAM R. JACK, B.Sc., M.D., F.R.E.P.S.P., Assistant Physician to the Western Infirmary of Glasgow. Fourth edition; Pp. 538. New York: William Wood & Co.

THE fourth edition of this small volume on the whole of the great subject of internal medicine, sets forth the salient features of disease in a careful and thorough manner. The book has been carefully revised since the last edition four years ago and has been brought up to date for the most part very satisfactorily. There are but few omissions of what is essential and but few mistakes or errors in the subject matter. The various diseases are dealt with in a most systematic though extremely dogmatic and didactic manner, as would be expected in a book of this type, so that it presents the subject of medicine in such a form as would be of practical value to a medical student. To a general practitioner, however, the value of such a book is extremely doubtful, certainly it would be of no real worth to a man, keen enough to desire to know more than the barest and brieflest facts about some unusual or interesting case.

J. H. M., JR.

PRINCIPLES OF HYGIENE: FOR STUDENTS, PHYSICIANS, AND HEALTH OFFICERS. By D. H. BERGEY, M.D., First Assistant, Laboratory of Hygiene and Assistant Professor of Bacteriology, University of Pennsylvania. Fifth edition; pp. 531; illustrated. Philadelphia and London: W. B. Saunders Company, 1915.

THIS new edition remains in aim and plan of arrangement the same excellent volume that its predecessor was, although many of the chapters have not been changed, still others dealing with subjects undergoing marked changes at the present time, have been revised and brought up to date.

This is especially true of that portion of the book dealing with the removal and disposal of sewage. Much of this chapter has been omitted, while a new diagram and some discussion of the

Emscher tank has been inserted. A new short chapter on nutritional diseases treats in brief fashion of beriberi, pellagra and scurvy. Antityphoid vaccination with an interesting reference to the results obtained in our own United States Army is a feature in this edition. A chapter on the transmission of relapsing fever and one covering interstate quarantine laws are additions worthy of note.

In the table of contents the divisions of body and foot inspection should exchange positions, and the page references should be corrected. These headings appear under the main chapter dealing with military hygiene, one which we are sure will be most thoroughly revised after the present struggle abroad. We hope the future sixth edition will continue to maintain the excellent standard of the present one. The book undoubtedly presents, as its author intends it to do, the practises of modern hygiene in a short, lucid, tangible style. The students in architecture, public health, sanitation, and medicine should find it a valuable aid in their work.

T. G. S.

DETECTION OF POISONS AND POWERFUL DRUGS. By DR. WILHELM AUTENREITH, Professor in the University of Freiburg. Translated by WILLIAM H. WARREN, Ph.D., Professor of Chemistry in Wheaton College. Fourth edition; pp. 320; 25 illustrations. Philadelphia: P. Blakiston's Son & Co., 1915.

TEN years have elapsed since the previous edition of this work was printed. The changes manifested in the present edition indicate the tremendous advance made in "Detection of Poisons." This new edition is larger than the last one by 100 pages.

The seven chapters now comprising the book have undoubtedly been painstakingly revised. The first three chapters remain unchanged only in arrangement. Such drugs as hydrastin, veronal, cantharidin, cytisin, ergot, papaverin, pilocarpin, saponin substances, salamin, thebarin, and the toxalbumins ricin, abrin, and crotin, are all discussed for the first time in these chapters.

The changes in the subsequent chapters have added very positively to the value of the book not only as a laboratory manual for students, but as a guide for those wishing to make practical use of the procedures described. Most that is new in the book appears in the fifth chapter, which treats of special methods in analysis.

The present edition is a faithful translation on the whole of the original German text. The translator has added, on a few occasions, some personal opinions to the subject matter of the parent treatise, *e. g.*, the introduction of the Gutseit method of estimating the quantity of arsenic and antimony. This present German edition has been translated into English, Spanish, and Italian—a

most complimentary tribute to any book, indicating the favorable manner in which it has generally been received. Both the author and translator have done their work well and have made a valuable contribution to medicine. T. G. S.

DIRECT LARYNGOSCOPY, BRONCHOSCOPY, AND ESOPHAGOSCOPY. By DR. W. BRÜNINGS. Translated and Edited by W. G. HOWARTH, Surgeon-in-Charge of the Throat Department at St. Thomas's Hospital. Pp. 367; 114 Illustrations. New York: William Wood & Co.

THIS book is a revised and expanded edition of Brüning's *Handbuch f. die Technik und Methodisk der directen Okularen Methoden*, and furnishes to the student in this comparatively new and rapidly expanding field of clinical work an excellent description of the necessary instruments and technique and the indications for their use. The first chapter, consisting of fifty-six pages, is devoted to the instruments which the author considers essential and their management. The indications for and the best methods of inducing anesthesia, local and general, are discussed, as well as the uses, advantages, and methods of giving oxygen inhalations. The remaining and greater portion of the book is devoted to the consideration of direct laryngoscopy, tracheobronchoscopy, and esophagoscopy, with sixty-seven pages on bronchoscopic operations and methods of treatment. The advances made in methods of direct inspection of these concealed portions of the body, particularly of the trachea and bronchi, are so important that not only the specialist but the general surgeon and physician will find it necessary to know more about them. It is interesting and important to know with what effectiveness local anesthesia can be employed in this method of investigation, that painting with a cocaine solution is more effective than spraying, and that a patient "had frequently been given as much as fifteen brushes of 20 per cent. cocaine solution," which is fifty times the so-called maximum dose. Direct exposure is rendering possible cures which were previously impossible. The passage of a bougie through a small eccentric opening in an esophageal stricture and the removal of a foreign body from a bronchus may now be done with precision and safety. The author is one of the acknowledged masters in this field, while the translator and editor has given us a lucid and readable translation which will be appreciated particularly by those who are fitting themselve for work in this special field. T. T. T.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Studies on the Mechanism of the Secretion of Urine.—E. LESCHKE (*Ztschr. f. klin. Med.*, 1914, lxxxi, 14) reports important experiments which he had made on the secretory activity of the kidneys, by means of histo-chemical tests which the author has devised. He is able to determine which cells secrete certain normal constituents of urine by methods which fix the solids in the cells. Thus, he has studied the secretion of chlorides, phosphates, urea and urates. He has also studied the secretion of iodide. His methods appear to be specific. It is only the cells which excrete these salts which show the reaction. By giving the experimental animals large quantities of water, the urine is so diluted that the specific reaction practically disappears, to become more intense, the more concentrated the urine is. The reactions are not found in other tissues except the stomach where the marginal cells show the chloride reaction; the chief cells lack it. The author summarizes his results and those reported in literature as follows: (1) Previous experiments to determine the mechanism of the excretion of dyes have shown that the greater part is excreted by the uriniferous tubules. To what extent the glomeruli are concerned remains unsettled. (2) The author's experiments, as well as those of other workers, have shown conclusively that salts foreign to the body (ferrocyanids and iodids) are excreted solely by the renal tubules, while the glomeruli themselves do not show evidence histo-chemically of excretion even when an excess of work is thrown upon the kidneys by injection of large amounts of salt. (3) By means of the author's histo-mechanical methods it is possible to demonstrate the point where the principle constituents of normal urine are excreted. (4) The excretion of chlorides, phosphates, urea, uric acid and purins takes place chiefly only in the specific excret-

ing cells of the convoluted tubules, and of the transitional portion connecting them with the descending straight tubules. Fahr's secretion granules, which disappear during hunger, are found in the same cells. (5) The glomeruli excrete water in physiological solution. The small quantities of salt and of other urinary solids corresponding to a physiological solution are also excreted by the glomeruli. (6) When the kidneys are forced to do increased work through injection of salt, urea, or purins, the excretion of the same is still exclusively by the same specific cells. The glomeruli, under these conditions, still excrete only water in physiological solution. (7) The ability to concentrate or dilute the urine rests entirely with the specific excreting cells or tubules. (8) Bowman's theory of the secretion of urine is fully confirmed. To what extent water is reabsorbed from the kidney's as Ludwig supposed, is undetermined.

On the Excretion of Creatin and Creatinin in Diabetics and Nephritics.—D. LAMPERT (*Ztschr. f. klin. Med.*, 1914, lxxx, 498) has made a study of the excretion of creatin and creatinin in diabetics and nephritics. He employed the Autenrieth and Müller method and all patients were on a meat-free and bouillon-free diet during the periods of observation. In healthy adults, he found the daily average excretion of creatinin to be between 0.9 and 2.4 gm., the majority being between 1.2 and 1.5 gm. Creatin was usually entirely absent, and, when present only in traces (0.02 mg.). In diabetics, the values for creatinin were usually lowered or at the lower limit of the normal. With few exceptions creatinin was found to an amount less than 1 gm. though in several cases 1 to 1.2 gm. was found. In diabetes gravis with a high grade of acetonuria, creatin was practically always found in the urine, usually more than 0.2 gm. (on two occasions 1 and 1.2 gm.). In diabetes levis with traces of acetone, creatin in two cases was lacking or present only in small amount (less than 0.3 gm.). In nephritics (five cases), the author found a decrease in creatinin constantly, even when there was a diuresis and only slight impairment of function. Creatin was found in only one case, in which there was marked renal insufficiency, and then only in small quantity (maximum 0.15 gm.). Two cases of diabetes complicated by chronic interstitial nephritis were characterized by an especially low creatinin value. Low creatinin values were also observed in a case of cancer of the liver with cholemia; creatin was also present in small amount (0.1 gm. or less). The author thinks it is plausible to attribute the large quantities of creatin found in the urine of diabetics with acidosis to a disturbance of metabolism and the diminished output of creatinin in nephritics to renal insufficiency. The generally accepted view that acidosis is the result of deficient oxidation of the acetone bodies suggests the idea that the increase in creatin is also due to a disturbance of intermediary metabolism. The findings in the nephritics suggest the use of this method in functional renal diagnosis.

On the Significance of Cholesterin in the Origin of Giant-cell Tumors of the Tendons and Joints.—S. WEIL (*Berl. klin. Wchnschr.*, 1915, lii, 129) refers to the recent work of several authors which have demonstrated an increase of cholesterin in the blood in patients having

xanthomas, even the simple lid xanthomas. In all of these lesions, the so-called xanthoma cells are found. Their dotted or foamy appearance is due to deposition of cholesterin. The author has been interested in the histological study of xanthosarcomata of tendons and joints. In a recent typical case, he had the blood examined for cholesterin, and it was found that it contained 0.27 mg. per c.c. (normal 0.14 to 0.16 mg. per c.c.). He suggests the need of further examination to determine whether this metabolic anomaly is constantly associated with the presence of xanthosarcomata.

The Therapeutic Use of Aqueous Extracts of Leukocytes in Lobar Pneumonia.—WILLIAMS and YOULAND (*Jour. Med. Research*, 1915, xxxi, 391) report the results of the treatment of seven cases of lobar pneumonia with aqueous extracts of leukocytes, as suggested by Hiss. In contradistinction to the reports of numerous other observers, the authors were unable to observe any definite evidence in their cases that such extracts exert a modifying influence upon the temperature and a lessening of the symptoms which are usually considered of toxemic origin. Of the seven patients, four died, and of these, two were alcoholic. They were unable to detect any differences in the results, whether the patients were given repeated uniform doses, steadily increasing doses, single moderate doses or single large doses, but in all patients, with one exception, the total amount of the extract used was large. No effects were observed upon the temperature, pulse or leukocyte count, regardless of how early in the disease the treatment was begun. The duration of the disease and the manner of its termination were about the same as one would observe in a similar series of untreated typical cases of lobar pneumonia.

Varieties of Pneumococcus and Their Relation to Lobar Pneumonia.—As the result of their studies, DOCHEZ and AVERY (*Jour. Exper. Med.*, 1915, xxi, 114) have shown that the pneumococci which can be isolated from individuals suffering from lobar pneumonia fall into four definite pathological groups which they have arbitrarily numbered from 1 to 4. The members of the first three groups appear to be related closely to each other, so far as one can judge from certain immunological reactions, while the members of the fourth group consist of independent varieties not definitely related to one another by the immune reactions employed. Thus far the authors have observed no change from one type into another nor any tendency of these organisms to lose their specific character. The groups vary distinctly in their pathogenicity for human beings, the order of their virulence being as follows: Groups 3, 2, 1, 4. On the other hand the degree of protective power which is developed in the sera of animals immunized against the various groups varies inversely with the virulence and the amount of capsular development. A careful study of the sputum from a series of normal individuals failed to reveal in any case an organism which could be grouped with any of the fixed types of pneumococcus. All of those found exhibited the same characters as those organisms which belonged to Group 4. These are of low virulence and cause only about 20 per cent. of the cases of pneumonia, hence it may be safely assumed that the majority of cases, particularly the more virulent ones, are due to organisms not

found in normal mouths. The only exceptions to this observation have been limited to a group of healthy individuals who have been intimately in contact with cases of lobar pneumonia. From such individuals organisms belonging to the typical groups have been isolated in a number of cases. Such individuals may safely be regarded as healthy carriers of disease-producing types. Dochez and Avery conclude from their study that probably the majority of the cases of pneumonia are dependent upon their direct or indirect contact with a previous case, that mere infection of the mouth by virulent types is not sufficient to cause the disease but that circumstances favorable to their invasion of the lungs must arise during the period when they are harbored in the mouth. From certain comparative studies they make the suggestion that strictly parasitic races of microörganisms are pure lines and have established themselves as parasites during a period of high racial susceptibility.

The Effect of Pituitary Extract upon the Secretion of the Cerebrospinal Fluid.—WEED and CUSHING (*Amer. Jour. Physiol.*, 1915, xxxvi, 77) have attempted to answer the question as to whether drugs which appear to increase the flow of the cerebrospinal fluid act directly on the choroid plexuses, or is their influence exerted on the cerebral capillaries in such a way that an increased amount of fluid is poured out through the perivascular lymphatics. In this study the authors have hit upon a far simpler method than those which have been previously employed. This consists of introducing a calibrated needle into the third ventricle by a callosal puncture. The experiments which are reported, were conducted either upon dogs or cats and all the injections were made intravenously. The results may be summarized as follows: when extracts of the posterior lobe of the hypophysis are introduced intravenously, they serve to discharge cerebrospinal fluid from the calibrated catheter introduced in its pathway. Positive results occur following the injection of nearly all the fluid proprietary preparations, but the dessicated extracts have tended to be more active. This increased secretion occurs under variable conditions and seems to be independent of respiratory or blood-pressure influences, for it has been observed to coincide with periods of respiratory cessation and in conditions of both hyper- and hypotension. An increased flow may even continue after the death of the animal. The evidence leads the authors to believe that the increased outflow under these experimental conditions represents the actual secretory response rather than an expulsion of preformed fluid, and they conclude that extracts of the posterior lobe of the hypophysis produce choroidorrhea by stimulating the secretory activity of the choroid plexus.

The Clinical Aspects of Syphilis of the Nervous System.—In a rather extensive article HEAD and FEARNSIDES (*Brain* 1914, xxxvii, 1) go over the very important subject of central nervous system syphilis, illustrating the various points which they wish to bring out, by suitable case records. The importance of a careful history of the primary infection, the early symptoms and signs of cerebrospinal syphilis, the serological findings in the various stages, and other valuable points are well brought out. These may be summarized as follows: All the manifestations of central nervous system syphilis are consequent on the direct

activity of Spirocheta pallida, and the clinical picture depends upon the situation of this activity and the susceptibility of the tissues. When the infection is mainly within the essential structures of the central nervous system, both neuroglia and nerve elements participate in the tissue reaction which results in the death and degeneration of certain systems of cells and fibers to which may be ascribed the greater part of the clinical manifestation. The authors believe that the more closely the clinical signs and symptoms point to pathological changes in the meninges and vessels, the more certainly will the disease yield to suitable treatment, while the reverse is true when the clinical symptoms point to one or more parenchymatous foci. The Wassermann reaction in the spinal fluid in the meningovascular form depends upon whether the spinal or basal meninges are involved, and the reaction tends to be negative or weakly positive when the disease is limited to the intracranial contents. In cases of syphilis centralis a strong Wassermann reaction is usually observed, as long as the disease is active. The former type of cases can usually be made Wassermann negative within six months under treatment with salvarsan or neosalvarsan, while the latter type is not apt to yield to any of the present forms of anti-syphilitic treatment. They are of the opinion that no complete diagnosis or prognosis can be made until the patient has been under observation and treatment for at least six months, during which time the cerebrospinal fluid has been systematically examined. No matter what the situation and nature of the lesion is, some secondary degeneration will almost certainly result and therefore some of the signs and symptoms are not apt to be altered by any treatment, hence the importance of making the diagnosis of syphilis early, so that therapy may be employed before the advent of the secondary stages.

Survival and Virulence of the Microörganism Cultivated from Polyomyelitic Tissues.—Flexner, Noguchi and Amos (*Jour. Exper. Med.*, 1915, xxi, 91) describe in the present paper a strain of the organism isolated from a case of polyomyelitis thirteen months ago. They are able to show the following interesting points: The organism has both survived and maintained its pathogenicity in cultures for over a year. Though the primary inoculation of this strain into monkeys may fail to produce polyomyelitis, the disease follows from the effects of successive injections and the lesions occurring in the spinal cord, medulla and ganglia are precisely the same as those which are found in the nervous system of animals which react to the injection of ordinary virus. The glycerinated nervous tissues derived from these monkeys which only develop the disease after several injections, are capable of transmitting the disease to monkeys upon intracerebral inoculation and from these animals the microörganism may be recultivated. The organism may be made to grow with difficulty under saprophytic conditions. Once this change has been affected, its growth occurs readily upon suitable media. If such an organism is reinoculated in the monkeys, the parasitic peculiarities of the microörganism are restored, for it then displays the marked fastidiousness to the artificial conditions of multiplication present at the original isolation. These experiments afford strong additional evidence in support of the view that this organism bears a close etiological relationship to the human and experimental polyomyelitis.

Isolation and Cultivation of the Tubercle Bacillus from the Sputum and Feces.—Dissatisfied with the lack of uniformly positive results when using the methods commonly employed, PETROFF (*Jour. Exper. Med.*, 1915, xxi, 38) has devised a new and simple method by which the isolation of the tubercle bacillus is rendered easy and certain. Thus 69 positive cultures were obtained from the sputum of 69 patients in all stages of tuberculosis. Of the specimens 6 were negative by direct microscopic examination; 19 positive cultures were isolated from 32 specimens of feces. From a series of experiments it was determined that a special medium containing gentian violet is the most satisfactory one to use. The details for the preparation of this medium are given in full. Moreover it is pointed out that under the most favorable conditions it takes at least six days for a single tubercle bacillus to grow to a visible colony. The method as applied to the isolation of the bacilli from the sputum consists in mixing equal parts of sputum and 3 per cent. sodium hydroxide. After being well shaken the mixture is placed in an incubator for a half-hour. It is then neutralized with normal sterile hydrochloric acid, centrifugalized, and the sediment inoculated in the media described. Most of the specimens gave positive results in seven days, though some took twelve to fourteen, but never longer. The colonies may appear violet, while others are capable of decolorizing the medium. A method for the isolation of the bacilli from the feces is described. It should be noted that the growth from the feces appears much more slowly than from the sputum, colonies appearing on the average of from two to three weeks after the inoculations are made.

SURGERY

UNDER THE CHARGE OF

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The Reformation of Gall-stones after Operation.—STANTON (*Ann. Surg.*, 1915, lxi, 226) says that notwithstanding the relative frequency of clinical recurrences following gall-stone operations, actual reformation of stones in the gall-bladder or ducts following their removal by operative methods is of extremely rare occurrence. He reports a case of definite reformation of stones in the gall-bladder after cholecystotomy and a general summary of the available data concerning this phase of gall-stone surgery. If no foreign body is left in the gall-bladder or ducts after the operation, the reformation of gall-stones is so rarely

observed as to constitute almost a negligible factor in gall-bladder surgery. The reported cases do not bear out the assumption that cholecystectomy affords a much greater immunity against reformation of calculi than does cholecystotomy. Adequate care should be exercised not to leave threads from gauze sponges nor unabsorbable suture material in the gall-bladder or ducts at the close of the operation. The data consulted during the preparation of this paper has further strengthened Stanton in the belief that the two most important factors in determining the end-results of gall-bladder surgery are the complete removal of the calculi and the maintaining of sufficiently prolonged postoperative drainage. In the absence of organic duct strictures he believes that the question of cholecystotomy *vs.* cholecystectomy is largely one of technical expediency in individual cases. In many badly diseased gall-bladders it is easier and safer to remove the gall-bladder than to try to remove all of the stones and fragments of stones from the gall-bladder *in situ*, and the same is often true of gall-bladders containing great numbers of minute stones and cholesterin particles.

Acute Hemorrhagic Pancreatitis.—Dyas (*Surg., Gynec. and Obst.*, 1915, xx, 211) says that a positive diagnosis of acute hemorrhagic pancreatitis cannot be made with absolute certainty, since we still lack a distinct pathognomonic sign for this disease. Laboratory aids, such as the Cammidge reaction and the Wohlgemuth diastase blood-test are of no value in this condition. A tentative or probable diagnosis can be made in a certain number of cases, provided a careful history is obtainable and the various phenomena, as they present themselves are properly interpreted. The most striking feature of this condition, clinically, is the evidence of peritoneal disturbance in the upper abdomen, the so-called "acute abdomen" which all surgeons agree is an indication for surgical interference; and acute hemorrhagic pancreatitis should always be borne in mind in such cases. When finding the peculiar odorless, serosanguineous fluid and the small flecks of fat necrosis, it is direct and undoubted evidence of acute hemorrhagic pancreatitis. The best results are obtained in cases in which operation precedes the stage of necrosis or pus formation. Hence, early surgical interference in all such cases will be rewarded by more frequent recoveries. The writer's personal observation of the intense cyanosis of the distended small intestines, with the peculiar granular or gritty feel of the thickened great omentum, has helped him in many cases to recognize the condition at operation, and look to the pancreas at once as the cause of the trouble. This is of special value in cases operated upon for supposed intestinal obstruction. The abdomen opened, the condition should be looked for and recognized quickly. Then prompt and sufficient drainage should be instituted, causing the patient as little shock as is compatible with good surgical technique. The high median incision is the best one to use, because it is the most favorable for exploratory purposes. The lumbar incision has its indications, but is only rarely resorted to, and then usually in late cases when abscess is pointing in the lumbar region. Postoperative hemorrhage is not an infrequent cause of death. It is due to necrosis, usually occurring in late cases. Therefore, early operation and gentle manipulation is the prophylactic treatment for this unfortunate complication.

Report of the Committee of the American Surgical Association on the End-results of Fractures.—Estes (*Ann. Surg.*, 1915, lxii, 278) as chairman reports for the committee the following recommendations: As a general principle fractures should be treated by a skilled surgeon. Roentgen-ray should be employed by a competent radiographer, or a fluoroscope should be used for diagnostic purposes before the permanent dressing is applied. At least two roentgenograms should be taken, and they should be taken from opposite perpendicular directions. Roentgenographs should be taken also after permanent dressings are applied to prove proper reduction, and at the end of the treatment to show the result of the union and for the purpose of a graphic record. Fractures should be reduced immediately after the injury if possible, to obtain and apply proper retaining apparatus or splints. The statistics show markedly better results when the treatment is begun at once. It is, however, not only useless but cruel to subject the patient to the pain of manipulation for reduction unless the surgeon has proper fixation apparatus at hand and the patient is where he may have a permanent dressing applied. General anesthesia should be employed as a rule to facilitate reduction and prevent pain, unless the condition of the patient contra-indicates it. Neither the operative nor the non-operative treatment is to be recommended exclusively. Each has its indication and should be employed when required. Generally speaking, the age period under fifteen years is the period in which non-operative methods are especially effectual. In the other age periods up to sixty years, operative methods may with confidence be employed when non-operative treatment has proved ineffectual in reducing, or controlling the fragments in proper position. The operations should not be delayed longer than one week after the injury. It may be used at any period, except in senile cases, whenever a roentgenogram shows a deformity or a position of the fragments which obviously cannot be reduced or when proper efforts at reduction and retention have proved unavailing. Some form of rigid plate applied directly to the bone or an Albee "inlay" seems to be the best fixation method in operative cases. Open operations for simple fractures should be undertaken only by experienced surgeons who are thoroughly equipped by training and who have proper instruments and apparatus to meet all the possibly indications of the operation.

Autoplastic Repair of Fractures of the Neck of the Femur.—Davison (*Ann. Surg.*, 1915, lxii, 284) reports two cases of fracture of the neck of the femur. In one patient, fifty-six years of age, a bone transplant was employed, and in another, fifty-four years of age, a large metal screw was used to fix the fragments. The first died twenty-three days after operation and the second, twenty-five days afterward. The pathological specimen from the first showed good union at the line of fracture, while that from the second showed only fibrous union. Davison concludes that: Autoplastic transplantation of bone is the best treatment for both recent and ununited fractures of the neck of the femur, unless contra-indicated by age or condition. The fibula furnishes the transplant of choice. The transplant impinging on the points of compact bone described will graft to these points of leverage

and give strong support to line of fracture. The transplant imbedded in cancellous bone will stimulate the production of osteoblasts and the growth of new semicompact bone in the cancellous area around the transplant, grafting them together by bony union. The transplant must be completely immobilized until it has grafted to the recipient bone. The position of immobilization must be extreme abduction and external rotation of the thigh. The plaster cast to be effective must extend from the axilla to the toes on the injured side and also include the opposite thigh in abduction.

The Treatment of Hip-joint Tuberculosis and its Results.—STOLLER (*Deutsch. Ztschr. f. Chir.*, 1915, cxxxiv, 54) studied the cases treated in Kocher's clinic in Bern and in his private clinic, between 1890 and 1913. Manninger collected and studied the cases treated between 1887 and 1900, but some of the cases between 1890 and 1900 were not at his disposal. Only such cases during this ten-year period are to be found in Stoller's group which include 63 cases in all. Of these, 31 were treated by radical operation, 8 by non-radical operations, 18 conservatively and 6 by osteotomy. The general and hygienic treatment was a very important factor. Under local treatment, he recommends the following: The mild cases are to be treated conservatively, as this is most likely to result in good healing. Rest and extension were especially favorable. But if complications arise, as suppuration, or if the conservative treatment is ineffective, operation should not be delayed any longer. The prognosis of operation depends much on the general condition of the patient. Garré operated only when life was in danger. Radical operations give good results with localized bone foci and sequestra. He advises against early operations because they are always very serious. They may lead to much shortening and increased lameness from injury to the bone without involvement of the epiphyseal line. The functional results from operative and conservative treatment are about the same, but after operation the shortening is greater. The results are not good from cutting and curetting fistulæ and abscesses without removal of the bone foci. Osteotomy for ankylosis gives good results and the danger of operation is about nil. It is difficult to say whether a movable or stiff joint should be striven for. A movable joint is most serviceable, but it must be used carefully. Therefore, the patient must be intelligent and under the control of a physician a long time. Ankylosis is less ideal but gives a good result for a working man.

A Case of Appendicitis with Ileocecal Intussusception.—LEDDERHOSE (*Deutsch. Ztschr. f. Chir.*, 1915, cxxxiv, 360) reports the following interesting case: A twenty-one year old under-officer was seized on the field with intestinal colic and dysentery and was taken to the hospital. The pain and straining movements of the bowels continued periodically and were associated with transitory abdominal tenderness and muscular rigidity in the right lower abdomen. Four weeks after the beginning of the trouble he developed the signs of acute appendicitis on account of which he was promptly operated on. The appendix was

the size of the thumb, brownish-red and tightly drawn from above downward. It passed through a sharp ring in the wall of the ascending colon and mesocolon. By careful pulling on the visible portion of the appendix it was gradually withdrawn and this was followed by the invaginated wall of the lowermost portion of the cecum and ileum. By this time the ring had disappeared. The appendix showed a strangulated ring but the cecum and ileum showed no signs of strangulation or stasis. The extirpated appendix showed subserous miliary pus foci and was tensely filled with pus. The mucus membrane was partly neurotic and the wall was nearly perforated at several places. Good healing followed the operation. Ledderhose believed the case one of chronic ileocecal invagination with acute appendicitis. Whether a causal relationship existed between intussusception and the appendicitis could not be decided.

Decapsulation of the Kidney for Bichloride of Mercury Poisoning.—LUXEMBOURG (*Deutsch. Ztschr. f. Chir.*, 1915, cxxxiv, 377) calls attention to Kummell's case in which the decapsulation of the right kidney for a complete anuria of seven days' duration, due to a severe poisoning, was followed in a few hours by the passage of 500 c.c. of urine and a larger quantity later. When the patient died eighteen hours after operation, she had passed over a liter of urine. Luxembourg reports four cases operated on by the late Professor Bardenheuer, of severe bichloride poisoning with good results. Tisseraud-Besancon operated on 3 cases of quicksilver poisoning with good results. Luxembourg concludes that in acute quicksilver poisoning, decapsulation of the kidney is a simple and not dangerous operation. As a consequence of the operation, the urine is again secreted. The decapsulation should be undertaken in all toxic nephrites from poison taken by the mouth and stomach, as soon as possible after the anuria has begun.

The Results of Eighty Pyelographies.—PLOTKIN (*Jour. d'urolog.*, 1915, vi, 431) says that pyelography or the study of the renal pelvis and ureter by means of roentgenographs after the injection of the ureter and pelvis with collargol solutions, has made possible the study of the pelvis, its various physiological anomalies and pathological changes. The beginning of a ptosis of the kidney is shown by the changed relation of the kidney to the last rib. A kink of the pelvis or a twist of the ureter is shown by the stagnation of the urine and the distention of the pelvis. In movable kidneys the calices preserve their normal form although distended, but when infection sets in the calices change. Pyelitis and pyelonephritis, due chiefly to the colon bacillus, cause dilatation of the calices and ulceration of the papillæ. Pyelography renders good services in disclosing congenital strictures of the ureter impassable to fine catheters and capable of causing hydronephrosis and severe colic simulating that of renal calculus. It is not of great importance in pronounced hydro- and pyonephrosis, because these conditions can be easily diagnosed by the clinical methods and the functional tests. It is valuable in the beginning of renal tuberculosis when the parenchyma is only mildly involved and the functional tests show nothing abnormal. It can show changes in the papillæ which habitually indicate the commencement of the tuberculous pro-

cess. In certain calculi permeable to the Roentgen-ray, the presence of the collargol cause a different shadow to appear at the site of the calculus. In the hands of experts, Plotkin considers that its use is without much danger. There is no more danger than in passing the ureteral catheter or lavage of the renal pelvis.

THERAPEUTICS

UNDER THE CHARGE OF

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Serum Treatment of Scarlet Fever.—REISS and HERTZ (*München. Med. Wchnschr.*, 1915, lxii, 1177) report further favorable results from the intravenous injection of mixed serum from several scarlet fever convalescents in the treatment of scarlet fever. They advise the intravenous injection of at least 50 c.c. for children and 100 c.c. for adults. The injections should be given as early as possible in the disease—to secure the best results. The serum to be injected is obtained from the donors between the eighteenth and twenty-fourth day of their disease. The donors should have preliminary Wassermann tests and tuberculous and septic patients should be excluded as donors. Reis and Hertz have occasionally observed the same beneficial effect following the injection of ordinary human serum, as convalescent serum, but much less often and consequently the use of ordinary serum for therapeutic purposes is more unreliable. Normal horse serum seemed entirely without any effect. The indications for this form of serotherapy are the severer toxic forms of scarlet fever, especially those cases with restlessness, delirium or evidences of heart weakness. In cases of scarlet fever where the toxic symptoms are due to secondary infection, serotherapy has no marked effect.

Treatment of Syphilis of the Brain.—IRELAND and WILSON (*Jour. Amer. Med. Assn.*, 1915, lxv, 1108), using the method of Byrnes, found that the intradural injection $\frac{1}{50}$ grain of mercury chloride in serum was safe. The reactions were a little more severe than following the Swift and Ellis method of 40 per cent. salvarsanized serum. They found that a clinical improvement usually appeared after about five treatments; 75 per cent. of their cases showed this improvement. A tendency to relapse to their former condition was observed in about 40 per cent. of those at first improved. They noted that clinical improvement was more marked and rapid than the serologic. Ireland and Wilson report a total of 23 cases with brief summaries of each case but note that their period of observation is too short to permit any definite conclusion regarding the permanency of benefit.

The Use of Calcium in the Treatment of Epilepsy.—Bryant (*Bost. Med. and Surg. Jour.*, 1915, clxxiii, 547) writes concerning the results obtained by the used of calcium in the treatment of epilepsy. The calcium treatment was combined with the usual bromide treatment. The official syrup of calcium lactophosphate was used in doses of from one to two drams three times a day. Bryant believes that calcium, in favorable cases, promotes sleep, decreases nervous irritability, and acts in some measure as an antidote to bromine acne. Nearly all cases have shown some benefit, in some very striking improvement followed the treatment. Calcium is not presented by Bryant as a panacea. He says it may not cure any case, but it at least can be said that when added to existing only parly successful treatment by bromides, it has in some cases produced results sufficiently encouraging to make it seem desirable to mention its employment and possible value.

The Clinical Type of Arthritis Originating about the Teeth.—Hartzell (*Jour. Amer. Med. Assn.*, 1915, lxv, 1093) has made bacteriological examinations of the teeth and peridental tissues in 220 patients suffering from arthritis. He has invariably found the Streptococcus viridans present not only in the confined dental abscess but also in the superficial tissues of the peridental membrane. The same results were obtained in the examination of the roots of normal lining teeth in a considerable series. Hartzell believes that the arthritis of dental origin is always due to a Streptococcus viridans infection. It is characterized by slow onset with more or less frequent exacerbations and remissions, which exacerbations seem coincident with the filling to distention of dental abscesses or retention of pus from deep pyorrhea pockets, which drain slowly into the circulation. Exacerbation frequently follows surgical treatment of pyorrhea or the curettage of alveolar abscesses. Treatment of pyorrhea pockets by curettage and evacuation of dental abscesses confers a double benefit. Such surgical interference necessarily inoculates the patient with a large number of organisms, inducing an effect similar to that of an efficient vaccine, with the added advantage that the constant supply is shut off from the focus disturbed. When many pyorrhea pockets or abscesses exist, it is important to permit from three to six days to intervene between treatments in order to gain the full advantage of what might be called surgical auto-inoculation. Certain it is that the above method brings about a constant and permanent gain generally ending in cure, whereas, if sudden complete extirpation of all foci is practiced as, for example, extraction of all the teeth at once, as is done in some instances, or extraction of all the teeth and removal of tonsils on the same day, the end-result will be positive harm. This type of arthritis is easily controlled when of dental origin, if the foci of infection are early recognized and eliminated. When, however, such foci obtain in an active state for a considerable period of time the disease becomes so firmly fixed that elimination of the primary focus does little in the way of repair, though elimination does limit further progress of the disease.

On the Treatment of Exophthalmic Goitre Especially in Relation to the Control of Protein Metabolism.—Boyd (*Edinburgh Med. Jour.*, 1915, xv, 108), after speaking briefly of general dietetic and hygienic

measures in the treatment of exophthalmic goitre says he has never been able to convince himself of any benefit following the use of belladonna. The same seems to apply to digitatis, strophanthus, and other cardiac tonics. The deleterious effects of iodide of potash or thyroid extract in Graves' disease are in most cases so pronounced and definite that in early cases when the diagnosis may be doubtful, their administration has been advocated as a means of establishing a diagnosis. The treatment of Graves' disease by preparations of the milk or blood of thyroidectomized sheep have not, in Boyd's experience, given satisfactory results. Boyd emphasizes particularly various measures to influence the excessive protein metabolism in exophthalmic goitre. He has found that extract of the whole adrenal gland has a certain definite influence in restraining the increased protein metabolism. The influence of parathyroid extract is but small and the impossibility of obtaining a reliable extract commercially precludes its clinical use. Radium is always useful but its general application is difficult and impossible in many cases. Treatment by Roentgen-rays is simple and often very effectual. A daily application for a week is followed in most cases by definite amelioration of symptoms. Excessive protein metabolism is restrained and the patient gains weight. The treatment can be repeated at the end of a month or six weeks.

The Treatment of High Blood-pressure.—Strauss (*Therap. Monatsh.* 1915, xxix, 10) says that it is important to distinguish between simple and complicated blood-pressure. He defines the latter as hypertension associated with subjective symptoms. In the cases of hypertension associated with sclerotic kidneys, the high blood-pressure seems to be compensatory and together with hypertrophy of the heart is necessary to enable the kidneys to excrete the incresed amount of urine. In such cases the aim of treatment is to protect the patient from useless overstrain of the heart and to guard against cerebral hemorrhage. Strauss warns against dietetic excesses, severe physical exertion and mental excitement or unrest as causative factors in hypertension. He advises elimination from the diet of all alcoholic stimulants, coffee, meat extractives, etc. With regard to medication Strauss states that small doses of digitalis, not over 0.1 gm. per day, are very useful and harmless in arteriosclerosis with high blood-pressure and beginning cardiac insufficiency. He has kept digitalis medication up for years with some of his patients, alternating two weeks of these small doses of digitalis with two weeks of iodin. The combination of a number of measures such as can be best carried out in a sanitorium—diet, baths, graduated exercises, etc , are especially beneficial in hypertension.

The Treatment of Paresis.—Read (*New York Med. Jour.*, 1915, cii, 561) has treated 20 cases of patients with 123 intralumbar injections of neosalvarsan, in doses ranging from 0.003 to 0.006 gm. diluted in at least 10 c.c. of the patient's own spinal fluid. During the treatment three patients died, but of these two were in the final stages and the deaths could not be fairly attributed to the treatment. One case, already slightly spastic when received, became intensely spastic and died with symptoms of motor tract degeneration. Two patients suffered incontinuence. A few complained of weakness, headache and leg

pains from time to time after treatment. One case developed a Charcot joint during treatment. One patient had convulsions following a treatment, but has had others not connected with the treatment. The Wassermann of the blood serum in 9 cases remained 4 plus. In two cases it is now negative, but in one it was negative before treatment and in the other it was not tested. One negative and one faintly positive Wassermann reaction in the spinal fluid have become strongly positive. The above are the infavorable results. The favorable results are the following: One case has entered a fair remission but still shows positive fluid findings. Another is improved markedly, but is still very evidently paretic. A number show improved conduct or physical health which may possibly be the result of hospital care. In 3 cases the Wassermann in the spinal fluid has become weaker. From the foregoing results Read concludes that the intralumbar treatment with neosalvarsan in smaller quantities is without effect and that when pushed with the object of obtaining results, it is extremely apt to prove injurious. Its use in this manner is to be discouraged.

The Use of Convalescent and Normal Blood in the Treatment of Scarlet Fever.—ZUIGHER (*Jour. Amer. Med. Assoc.*, 1915, lxv, 875) reports the results obtained in treating twenty-three scarlet fever patients at the Willard Parker Hospital with intramuscular injections of blood. This group of patients represent the cases with the poorest prognosis, selected out of a total of some nine hundred admissions. Fifteen were treated with convalescent blood, which was citrated in a majority of cases. Nine received blood from two or more donors. The amount injected varied from $2\frac{1}{2}$ to 8 ounces. Of the fifteen patients, four died; of these (*a*) one died from septic bronchopneumonia two days after the injection; (*b*) one died of a streptococcus sepsis nine days after the injection; (*c*) one was moribund when injected intravenously. He seemed to rally slightly, but the treatment was evidently given at a time when the patient's nervous system was entirely overwhelmed by the toxemia; (*d*) the fourth patient, practically moribund at time of injection, had severe meningismus with a marked retraction of the head; he died thirty-six hours after injection. Of the eleven patients who recovered only five were of the purely toxic type; the remaining six patients had additional severe septic complications, especially tonsillar and faucial exudates, and inflamed cervical glands. The five purely toxic cases showed a critical drop in temperature which varied from 3° to 6° F., after which the temperature remained normal or slightly above normal. In the remaining six cases, the drop in temperature was less marked and was followed by a secondary rise which persisted for a number of days. These secondary temperatures were evidently due to the septic complications. Eight patients received fresh normal blood; of this group, none died. These cases were far advanced septic cases, several with a poor prognosis. The blood, which was readily obtained from one or both of the parents, was citrated in six. One of the patients received two injections of 6 ounces each; another three injections, each of 8 ounces at intervals of four or five days. As was to be expected, no striking critical drop but a distinct lowering of the temperature curve was noted, associated with an improvement in the septic complications and the general condition

of the patient. The good results in some of these cases are the best proof of the beneficial effect that can be derived from this treatment. While it is difficult to make any absolute statement or arrive at definite deductions from such a small series of cases, one can only hope that, by continuing this form of treatment, a larger series of cases may finally be collected that will serve as a more definite guide for the value of the intramuscular injections of convalescent and normal blood. The treatment is easily carried out, is quite harmless, and is within the reach of the general practitioner. The beneficial effects noted in the above groups of very severe cases were quite distinct. The rational element in the use of convalescent blood is apparent, so long as the etiology of scarlet fever is not known, and the use of antistreptococcus serum during the past ten years has not given the striking results that were expected from it after the early trials. The rational element in the use of fresh normal blood in the septic cases is found, first of all, in clinical observations of its great empiric value; but also to a large extent, in a consideration of the great nutritive value of homologous blood, its marked stimulating properties, and its well-known antibody content which exerts a distinct bactericidal effect on many pathogenic organisms.

Fatalities after Salvarsan.—FISCHER (*Deutsch. med. Wchnschr.*, 1915, xli, 908, 939, 976) summarizes his long serial article regarding the reported cases of fatalities following salvarsan as follows: The only injuries from salvarsan actually demonstrated at the present time are local necrosis at the point of the injection, and hemorrhagic encephalitis. Many accidents including death have followed salvarsan injections, but most have not been due to the medication. In a number of instances the fatal result has been determined by coincident disease. He cites as examples one case of generalized tuberculosis, with both suprarenal glands destroyed that died soon after salvarsan treatment; in a second case the fatal result seemed to be due to a coincident recent abortion and hemorrhage and in a third case an unsuspected pneumonia was found. Among the fatalities ascribed to salvarsan are cases in which no lesions, not even microscopic, could be found at autopsy and no evidence of toxic chemical action could be discovered. In one case chemical investigation revealed evidences of mercurial poisoning and Fischer believes that some of the fatal cases are probably more likely due to mercurial poisoning rather than to poisoning with salvarsan. He claims that there is no evidence that salvarsan has a toxic action on the liver cells. In those cases developing an acute yellow atrophy of the liver following salvarsan injections he believes that the degeneration of the liver is due directly to the virus of syphilis and not to the toxic action of salvarsan. The poisonous action of salvarsan does not correspond to the clinical picture of arsenic poisoning. He says that cases which appear to justify this conclusion have been imperfectly studied.

The Treatment of Syphilis with Salvarsan Alone.—KREFTING (*Deutsch. med. Wchnschr.*, 1915, xli, 979) claims that mercury adds nothing to the efficacy of salvarsan in the treatment of syphilis. He believes that primary syphilis can almost certainly be cured with

from three to five injections of salvarsan at intervals of fourteen days. He advocates using large doses when treating early stages of syphilis. He says that definite rules for the salvarsan treatment of secondary syphilis cannot be made. The treatment must be individualized using the remedy in smaller doses than when treating primary syphilis. Salvarsan treatment should be used over prolonged periods of time and should be persisted in for some time after the Wassermann reaction becomes negative.

PEDIATRICS

UNDER THE CHARGE OF

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Mumps: A Critical Review.—FEILING (*Quart. Jour. Med.*, 1915 viii, 255) states that this disease often belies its supposedly benign character as shown by recent advances in the knowledge, especially, of its complications and especially that of the nervous system. The disease may occur without acute inflammation of the parotid gland. The age incidence reaches its maximum between the fifth and fifteenth years, but no age is exempt. The mortality is extremely low. There is a prodromal stage before the appearance of the characteristic parotitis, during which infection is possible. This stage is probably four days long. The duration of the contagion is probably three weeks from the onset of the disease, although Sharp reports two cases remaining infectious for six weeks. The causal organism of mumps has not been satisfactorily isolated. Nicolle and Conseille by injecting fluid from parotid glands of patients with mumps into the parotid glands of monkeys apparently have demonstrated transmission of the disease, the occurrence of immunity following it and blood changes similar to those found in the human patient. No organisms were found. Gordon's experiments along similar lines with monkeys showed distinct changes in the nervous system such as lymphocytic infiltration and nerve cell degeneration. He concludes that mumps is apparently due to a filterable virus comparable to that of poliomyelitis, smallpox, and typhus; that the virus can pass through a Berkefeld filter and is destroyed at 55° C. Feiling gives the changes in the blood as a slight increase in the total number of leukocytes; a lymphocytosis both relative and absolute which persists from the first day for at least fourteen days. The occurrence of orchitis does not invariably alter the blood picture. The blood changes are of distinct value in differentiating mumps from other inflammatory swellings of the parotid or submaxillary salivary gland. The complications affecting more frequently adults are grouped as follows: Abnormal modes of onset, such as testicular involvement preceeding the parotitis or meningeal symptoms ushering in the disease; orchitis followed frequently by atrophy; pancreatitis, the commonest cause of which, in children, is probably mumps; nervous symptoms,

including meningeal symptoms, rarely meningitis, and a marked lymphocytosis of the cerebrospinal fluid; lesions of the cranial and peripheral nerves including facial paralysis, herpetic eruption, and toxic polyneuritis.

Whole Milk in Artificial Feeding of Infants.—VINING (*The Practitioner*, 1915, xcv, 589) makes a plea for the more frequent use of whole milk in artificial infant feeding and claims that the frequency of rickets is partly due to wrong methods of feeding, especially dilution in modified forms of feeding and the use of proprietary foods. He suggests whole milk feeding in all cases where the natural supply is not available. In discussing the usual objections to whole milk feeding the author claims that the difficulty in using whole milk lies in the mechanical factor of clot formation and that the use of heat (110°) or the addition of sodium citrate prevents clot formation and makes this form of feeding successful. The addition of sodium citrate has no effect of drugging as cow's milk normally contains sodium chloride and citric acid. The constipation met with in whole-milk feeding is not due to the sodium citrate as the same condition occurs in breast-fed infants. As to dried milk, the author claims that fresh milk may be sterilized by heating and if there is any risk of scurvy in either it would seem to lie in the use of dried milk. The dried milks, however, are superior to the proprietary foods. Babies can be fed successfully on whole milk containing sodium citrate from one to two grains to the ounce at any time after the first month. As to the amount to be used the best method is to allow the baby to indicate the amount it requires, the amount varying naturally at different feedings, and to check this by observing the condition of the stools, the amount of sleep, its weight and physical development. Constipation must be avoided and liquid paraffin or equal parts of the confections of sulphur and senna are recommended.

Radiography of the Thorax in Children.—FOWLER (*Edinburgh Med. Jour.*, 1915, xv, 326) offers a number of case histories to demonstrate the value of radiography of the chest in children for determining particularly tuberculous changes. The diagnosis of miliary tuberculosis in children is often difficult and frequently the radiograph shows lesions that show no clinical signs. The radiograph is, however, usually characteristic and affords probably the earliest means of making a correct diagnosis. One of the cited cases was a child of eleven years who ran a slight temperature, and lost weight four months after a serious pleurisy which could not be proven tuberculous. Physical signs showed no evidences of lung involvement, but a radiograph showed extensive miliary tuberculosis. Another case in a boy of five years was investigated by Roentgen-rays because a sister had had the disease. The boy showed no particular clinical signs and yet the radiograph showed a considerable mottling throughout the chest and a large shadow in the scapular region. He subsequently developed active tuberculosis and another radiograph showed quite an increase in the lesions. Exudates into the pleural cavity give a well-marked shadow. Fowler reports the case of a child of nine years with fever, headache and pain in the epigastrium which was not diagnosed for

some time when a radiograph showed a shadow over the left lung indicating pleurisy with lymph formation. From these facts gained from time to time the author places the radiograph very high in the diagnostic methods employed in conditions of the thorax in children.

Gastric Radioscopy in Children.—Willox (*The Practitioner*, 1915, xcv, 599) gives a very minute and detailed account of his study of radioscopy on the stomach of the child. Every phase of the subject is discussed, the method, time, substance used, position of the child, etc. The objects were to determine the shape and general appearance of the stomach after a meal, the effect of different foodstuffs on motility, the rate of passage and the average time of emptying. From the author's summary of his investigation we find that the shape of the stomach with contents varies with the process of digestion, but that in general it is globular becoming elongated as the child ages, so that in older children immediately after a meal the stomach is of an "F" shape, resembling a Dutchman's wooden shoe. Foodstuff of itself has little if any effect on motility. Fluidity is the determining factor, the more fluid a meal is the more quickly will it pass through the stomach. Equal parts of milk and lime water pass more quickly than milk alone. Citrated milk goes through more quickly than plain milk. Stomachs of older children empty as quickly as those of younger children, provided the meal is similar in bulk and consistence. In some cases food begins to pass the pylorus as soon as the meal is taken, in some a resting stage occurs before peristalsis begins. The average time for the stomach to become empty was three and three-quarter hours. Porridge or bread and milk are the best media for either the barium sulphate or the bismuth, neither substance sets up intestinal disturbance. There is no evidence that bismuth forms a coating for intestinal mucous membrane. The stomach lies high up in the left hypochondrium in infants. The food passes the pylorus intermittently and in an apparently nodular form.

New Features in the Diagnosis of Scurvy.—Alan Brown (*Arch. Pediat.*, 1915, xxxii, 744) in discussing the metabolism of scurvy points out some important features in the diagnosis of scurvy. The important points are fever, leukocytosis, great radiability of recently extravagated blood and the "white line." A high temperature and a leukocytosis, even as high as 26,000, occur in the severe and more advanced cases of scurvy where a faulty diagnosis of pus is apt to be made. The demonstration by Roentgen-rays of the "white line" is a valuable check to this diagnosis since the white line at the junction of the epiphysis and diaphasis occurs in scurvy even before the cardinal symptoms of the disease appear and represents an increased density at that point. The author has confirmed the findings of Talbot, that the "white line" is a constant sign of infantile scurvy that it may persist months after complete clinical cure and that it is of decided value in making an early diagnosis and instituting treatment. The production of this line is by hemorrhage between the diaphysis and epiphysis. The apparent difficulty at times of differentiating by Roentgen-rays between a recent subperiosteal hemorrhage and pus is caused by the greater radiability of recently extravasated blood over that which has already

begun to organize. The subperiosteal hemorrhage takes weeks or months to completely organize. In one of the author's cases complete absorption had not taken place at the end of five months. The absence of subperiosteal hemorrhage as shown by the Roentgen-rays does not therefore exclude scurvy. In scurvy fine petechial spots may usher in the prescorbutic stage. By applying a blood pressure cuff and 90 mm. of mercury minute petechiæ occur below the constriction in scorbutic patients (Hess). The "exudative diathesis" is associated so constantly with scurvy that Brown claims a close inter-relationship between the two and that the former implies a diathesis for the development of scurvy. The only etiological factor yet known in scurvy is diet and the most prominent foods are proprietary infant foods, condensed and sterilized milk. Scurvy is an exceedingly rare result of pasteurization. Sterilized milk, by the heating alone, causes a large number of cases.

OBSTETRICS

UNDER THE CHARGE OF

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The Use of Preparations of the Hypophysis in Obstetric Practice.—Vogt (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, lxxvi) gives the results of his observations in the Dresden Clinic. He calls attention to the familiar facts that where the birth canal is dilated and dilatable, the position and presentation favorable, all that is needed is vigorous uterine contraction, that this substance will produce prompt uterine action and thus terminate labor. He draws attention to the fact that symptoms of threatened uterine rupture furnish a positive indication against its use. So do the symptoms and all indications of overdistension of the uterus. He mentions a case of transverse presentation with prolapse of the arm, where no diagnosis was made and pituitrin was given, followed by rupture of the uterus, which terminated fatally. Repeated doses do not seem to act in a cumulative manner; the drug can be repeated in from one to two hours during all the stages of labor. There are patients who bear it badly, in whom after the use of the drug, the pupils dilate, the pulse grows slow, there are symptoms of collapse, paleness, giddiness, prostration and cold sweat. If also the drug is given rapidly by intravenous injection in too large a dose, these symptoms may follow. In multiparæ, during the period of expulsion, the drug may cause very severe pains, which probably come from cramp-like contraction of the uterine muscle. This can be controlled by some preparation of opium, which does not seem to prolong the labor. The action of the drug may also cause formation of stricture and tetanus of the uterine muscle at the internal os. It would thus be a mistake to administer the drug before performing version or when it was necessary to dilate the lower portion of the uterus. In

some cases the uterine muscle seems exhausted by this preparation and atony of the uterus is observed afterward. The child's heart sounds are prolonged when pituitrin is given, and sometimes may be reduced to 80 or even 40 beats to the minute. The sounds are less distinct, the meconium is sometimes expelled, and the child may die from excessive pressure during birth. If pituitrin is to be employed the heart sounds should be carefully observed during the labor. These observations are based upon 7600 labors, with preparations of the hypophysis, manufactured by an American firm, an English firm, a French manufacturer and a German chemist.

The Cause and Treatment of Transverse Position of the Fetal Head Complicating Labor.—MARTIUS (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, lxxvi) reviews the literature of the subject and has gathered statistics and adds the results of his observations in the Clinic of Bonn. He thinks that great variations are present in the way in which the body of the child engages and passes through the pelvis. When the pelvic brim is a long oval and the head of the child corresponds to this peculiar formation, transverse position frequently develops. In some cases the elements which produce anterior rotation seem to be entirely lacking, the pelvis is without its normal contour, the head is rounded so that it does not fit the pelvis, and in some cases it is much smaller than the pelvis. In others the pelvis may be flattened, or the child may present by a parietal bone, and thus anterior rotation may be hindered. In five out of six cases, where no great disproportion exists between the head and the pelvis, labor will terminate spontaneously. It is best not to attempt anterior rotation by any manipulation, even though the pelvis should be somewhat abnormal. In flat pelves, if the head permits considerable compression in the biparietal diameter, successful labor may still result. Where there is difficulty in the passage of the head through the pelvic brim, Walcher's position is especially valuable.

Absorption from the Genital Tract during the Puerperal Period.—AHLFELD (*Ztschr. f. Geburtsh. u. Gynäk.*, 1915, lxxvi) has conducted a long series of experiments to determine the question of absorption from the genital tract during the puerperal period. He concludes that at no time in pregnancy, labor or in the puerperal period does the absorption of material from the genital tract go on from the vagina and from the uterus at the same time. Independently of the size of the uterine cavity, absorption from the contracted uterus is diminished and from the relaxed uterus is increased. On the third, fourth, fifth and sixth days of the puerperal period absorption from the inner surface of the uterus reaches its highest point. As the uterus undergoes involution, from this time on the absorption steadily diminishes. When from any pathological condition the uterus remains greatly relaxed after the sixth day, absorption takes place with great freedom.

Nephrectomy during Pregnancy.—SCHMIDT (*Surg., Gynec. and Obst.*, December, 1915, reports the case of a multipara, aged twenty-eight years, who had renal infection with the B. colon and B. tuberculosis. The left kidney could be palpated as enlarged and sensitive. The patient was pregnant at about the end of the fifth month. The kidney

was removed through the usual incision, the ureter and vessels being separately ligated and the wound closed, except for both ends of the incision. The patient made a slow recovery, drainage persisting at the lower angle of the wound until after the childbirth. The patient had a normal labor but the baby died twelve days later of septic infection. On pathological examination the kidney was tuberculous with pyonephritis and ureteritis. Schmidt has in all collected 35 cases with a maternal mortality of two mothers (5.7 per cent.). In 77 per cent. labor was normal at term. In 15 per cent. the results of the operation were harmful upon the fetus. Three of these patients had spontaneous abortion: one induced abortion, one induced labor, one dead fetus extracted. As regards the time of operation, the greatest number of cases occurred in the fourth month of pregnancy; then in the fifth; then in the sixth. The remaining months had about the same number of cases. Especial attention must be given to the maintenance of function in the remaining kidney in a pregnant woman. Should this fail the uterus must immediately be emptied. The writer believes from a study of the subject that a woman with one absolutely healthy kidney and no constitutional infection may safely marry and incur the risks of pregnancy. He reports in detail the 35 cases collected and his own (36 in all). The reviewer recently had occasion to observe the patient admitted to the Maternity of the Jefferson Hospital suffering from eclampsia, one of whose kidneys had been removed for tuberculous infection. The patient recovered from the eclamptic seizure although the child succumbed. So far as could be ascertained, her recovery was complete and she reacted to treatment as well as other cases where both kidneys were present.

Premature Separation of the Normally Implanted Placenta.—Williams (*Surg., Gynec. and Obst.*, November, 1915) in a paper on this subject states that in 2000 labors at the Johns Hopkins Hospital, antipartum hemorrhage was noted in 17 and placenta previa in 14 cases. As regards the cause of separation of the placeata, trauma is admitted; mental emotions have never been recognized, while a toxemic process is very frequently present. A change in the consistence of the uterus is a striking symptom. When the natural physiological alternation between contraction and relaxation is absent, the diagnosis is practically assured. The uterus remains hard and more or less painful and this condition is independent of concealed or external hemorrhage. An examination of the blood and the recognition of changes in the hemoglobin percentage will give valuable indications of danger, often before the pulse shows evidence of shock. Williams reports two cases treated by Cesarean section, with the recovery of the mothers. The children were dead at the time of operation. In the first case the uterus failed to contract and the operation was terminated with hysterectomy. A similar procedure was carried out in the second and, in both cases, a necrobatic process in the muscular tissue of the uterus, described in 1911 by Couvelaire was demonstrable. While opinions may differ as to the precise pathology which examination of the specimens shows, in these cases there is clinical evidence of their association with a toxemic condition. Williams concludes that premature separation of the normally implanted placenta occurs more frequently than is

generally believed and may give rise to only trifling symptoms or may endanger the life of the patient. In severe cases the accident is associated with profound disorganization of the uterine muscle, by hemorrhage (called by some observers uteroplacental apoplexy). An undifferentiated form of toxemia is the probable cause and this may or may not be accompanied by albuminuria. As regards treatment, some cases terminate successfully spontaneously; in others labor must be induced and in others immediate operation is necessary. If the bleeding be but slight or the symptoms of separation be not pronounced, the patient may be put under observation, with the hope that nature will deal successfully with the case. If bleeding is profuse and the cervix admits easy dilatation or is already partially dilated, the use of a dilatation pack followed by forceps may be indicated. Where the cervix is but slightly dilated, abdominal Cesarean section is the operation of choice. Should hemorrhage occur after the uterus is emptied, it should be packed firmly with gauze and if this is unsuccessful the abdomen should be opened and hysterectomy done. So far as rupturing the membranes or tamponning the vagina is concerned, neither is advised. When the diagnosis of concealed accidental hemorrhage can be made Cesarean section is the operation of choice, except in the rare cases where the cervix is fully dilated and the conditions favorable for vaginal delivery. The reviewer has for some years treated such cases by abdominal Cesarean section with good results. He has twice performed hysterectomy for the condition described by Couvelaire and Williams. In one instance the placenta had been normally situated but separated and in the second a partial placenta previa was present. In both the mothers recovered but the children were dead at the time of operation.

Obstetrics — A Lost Art. — HOLMES (*Surg., Gynec. and Obst.*, November, 1915) contributes a paper under this title, in which he criticizes the improper performance of Cesarean section. He argues that contracted pelvis alone is the definitely permanent indication for the operation; that the baby must be in good condition unless there is no other way of delivering safely, under any circumstances the fetal body. He would exclude eclampsia, placenta previa and believes that in the lesser grades of pelvic contraction the test of labor should be employed. Where the indication is absolute, labor should be avoided. Unless the patient be a multipara with a relaxed pelvic floor, a Cesarean section on one occasion would render necessary its performance for any subsequent pregnancy. He believes that the mortality of 5 or more per cent. for Cesarean section is too high. Many of the points in this paper are well taken but the experience of the reviewer does not coincide with the arguments advanced by the writer of the paper. We have repeatedly seen women who have previously had Cesarean section deliver themselves spontaneously and safely of living children. A mortality of 5 per cent. in clean cases is certainly excessive but if the desperate cases or sepsis and rupture of the uterus complicating contracted pelvis be considered, the mortality will inevitably be more than 5 per cent.

Acute Inversion of the Puerperal Uterus.—Jaschke (*Zentralbl. f. Gynäk.*, 1915, xxxii) describes the case of a multipara, aged twenty-nine years, who had in one previous labor been delivered by forceps. The history stated that in four preceding pregnancies the placenta had to be removed manually at the time of labor. After her last pregnancy there was a severe hemorrhage on the twelfth day of the puerperal period. The patient was admitted to clinic two weeks before labor. She had varicose veins on the right thigh at the lower portion and the tissues of the thigh were considerably thickened. Labor proceeded rapidly and easily and a few moments after the expulsion of the child uterine hemorrhage occurred. The uterus was relaxed and Credé's method of placental delivery was employed in the effort to make the uterus contract. As the placenta did not separate it was removed by the hand and found to be adherent at the fundus and anterior wall of the uterus. On removing the hand without making traction upon the placenta and exercising the greatest possible gentleness, the uterus inverted itself completely. When the writer arrived, he found the uterus entirely inverted and outside the vulva and a portion of the placenta firmly adherent to the fundus. Hemorrhage had ceased with the inversion of the uterus. The patient was in severe collapse. Iodine was at once applied to the vulva as an antiseptic, the portion of placenta separated, the uterus replaced, when, upon withdrawing the fingers, the uterus again showed a tendency to inversion. This, however, was checked and the uterus tamponed firmly with gauze, when hemorrhage entirely ceased. Counter pressure was made by a firm abdominal bandage and a pad. In the puerperal period the patient had thrombosis of the veins of the right leg which could be traced to varicose veins on her side. The patient made a tedious but complete recovery.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF

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Cerebrospinal Meningitis and the Sphenoid Sinus.—Peters (*Jour. Laryngol., Rhinol., and Otol.*, July, 1915) and others report cases illustrating the intranasal conditions existent in cerebrospinal meningitis. As commented upon editorially Peters suggests that the sphenoidal sinus disease tends to lead on to meningitis if the orificial outlet of the sinus becomes blocked, and that therefore free drainage should be secured by the procedures familiar to the modern rhinologist.

Buttermilk Gargle in Diphtheria.—Moffitt (*Pennsylvania Med. Jour.*, October, 1915) reports that in nine patients in whose throats diphtheritic bacteria remained after all other manifestations of the

disease had disappeared, buttermilk was used five or six times daily as a gargle. In eight of these cases an almost pure culture of lactic acid bacilli were found on the third day after beginning the procedure, no diphtheria bacilli being present. In the ninth case cultures on the fifth day showed a pure culture of lactic and bacilli.

Pharyngeal Fistula after Operation on Abscess in the Neck.—HARMER (*Jour. Laryngol., Rhinol., and Otol.*, October, 1915) reports a glandular abscess which formed in the neck of a man shortly after a prostatectomy. Ten days after incision of the abscess there was paralysis of the palate with regurgitation of fluid through the nose, and soon afterward food passed from the mouth through the wound in the neck. As the abscess was not draining well the opening was enlarged. The wound in the neck and the suprapubic wound were both healing sluggishly at the date of the report.

Functional Aphonia following the Bursting of a Shell in Close Proximity to the Patient.—TILLEY (*Jour. Laryngol., Rhinol., and Otol.*, October, 1915) reports two cases. The first one was that of a man, near whom a shell had burst on November 5 rendering him aphonic until December 11. The second case was that of a man who had been buried by a "Jack Johnson" for four hours. When dug out it was found that his voice had gone and likewise his hearing. He remained thus for three months and was sent into the hospital. In neither patient could any other morbid condition be found, while inquiry showed that the voice had been strong before the accidents. The first patient got well in response to a moderate intralaryngeal faradic shock. But even a strong faradic shock did not restore phonation in the second case. As the patient refused to open his mouth the laryngeal electrode was passed through the left nasal cavity into the larynx, and the current increased until the resulting spasm induced marked cyanosis. On removal of the electrode the patient's voice returned, and he spoke for the first time in three months. His hearing was also returned. These faculties had not been lost since, but the general condition might be described as that of profound neurasthenia. O'MALLEY (*Ibid.*) reports six cases of functional aphonia which had come under his own care, all having occurred in the trenches. In four the voice returned on asking the patient to phonate with the laryngoscopic mirror in position for the purpose of examination. In the other two a mild application of the faradic current proved effective. WHALE (*Ibid.*) reports a case of sudden aphonia in the trenches without any history of injury. The movements of the vocal cords were perfect, but there was cessation of expiration on their adduction. There was sudden recovery from the neurosis in twenty-four hours.

Malignant Tumor at the Base of Tongue almost Dispersed by Radium.—HILL (*Jour. Laryngol., Rhinol., and Otol.*, October, 1915) reports the case of a male subject, fifty-five years of age, with a growth the size of a walnut ulcerating posteriorly, and with secondary involvement beneath the left angle of the jaw. The left side of the tongue was fixed. There was accasional hemorrhage, and in addition salivation, dysphagia, constant pain and insomnia. The treatment was by in-

sertion in two places of small, hollow, needle-like emanation apparatus of platinum 0.3 mm. in thickness, containing an initial charge equivalent to 40 mg. of radium bromide for twenty hours altogether. All symptoms had disappeared, and the tumor had become so reduced that it might easily be overlooked on superficial exploration.

Tuberculosis of the Frontal Sinus.—THOMAS (*Jour. Amer. Med. Assn.*, July 24, 1915) in reporting two personal cases states that but five in all had been reported previously, and gives a synopsis of these cases. Four of the five terminated fatally, and the other one had remained well for seven months after operation. Of the reporter's cases one recovered after two operations and had remained well for more than two years. The other case had been subjected to extensive intranasal operation two years before Dr. Thomas was consulted. It is reported as a case of "tuberculous frontal sinusitis with osteomyelitis, epidural, subdural and cerebral abscesses, resulting in death, a necropsy being held."

Trichinosis Simulating Frontal Sinusitis.—PRATT (*Jour. Amer. Med. Assn.*, October 9, 1915) reports three instances occurring in his practice during the past two years. He has not found mention of any similar cases after a very comprehensive search of the literature. Two cases were in females aged thirty-one and thirty-two years, respectively, but the age of the male patient is not stated. The diagnosis in all three cases rested on (1) edema of the lids with absence of edema elsewhere; (2) negative nasal findings referable to the accessory sinuses; (3) the history; and (4) the proportion of eosinophiles (22 per cent., 20 per cent., 6 per cent., and afterward 20 per cent., respectively). In all these the presenting symptom was pain in the region of the eye and frontal sinus.

Laryngeal Stenosis and Collateral Injuries from Shrapnel, Bullet, and Bayonet Wounds.—A number of interesting cases were reported before the Laryngological Section of the Royal Society of Medicine (*Jour. of Laryngol., Rhinol., and Otol.*, October, 15) to which the reader must be referred for detail and discussion.

Glosso-laryngo-scapulo-pharyngeal Hemiplegia following Gunshot Wound Behind the Right Mastoid.—COLLETT (*Ann. de Mal. de l'oreille, du larynx, du nez et du pharynx*, August, 1915) reports this case in much detail. He stats in conclusion that a glance at the base of a cranium shows that this new type of associated laryngeal hemiplegia could be produced by a lesion barely a centimeter in diameter, localized in front of the occipital condyle in such a way as to involve the affected cranial nerves, passing through the posterior lacerum, anterior condyloid and carotid foramina.

Paralysis of the left Recurrent Laryngeal Nerve due to Mitral Stenosis.—GUTTMAN (*The Larynscope*, August, 1915) reports this case in a woman, aged twenty-six years, who had suffered with rheumatism seven years previously. There was a marked difference between the two radial pulses. Fluoroscopic examination revealed a markedly

dilated pulmonary artery, which, by pressure against the recurrent laryngeal nerve and against the aorta itself, produced the laryngeal paralysis and diminished the blood supply to the left upper extremity.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

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Tuberculosis of the Female Genitalia in Childhood.—GRAEFE (*Inaug. Dissert.*, Halle, 1914) had an opportunity of observing 19 cases in children and comes to the following conclusions: Tuberculosis of the genitalia is much less common in children than in adults, but when found, appears more frequently to fall between the ages of one to five and ten to fifteen. These tuberculous foci are secondary to older lesions in other parts of the body and arise through a hematogenous infection. It is more common in the tube and uterus and rare in the ovary, vagina and vulva. The tuberculous process begins in the mucous membranes of the tube and uterus and from here extends into neighboring parts. Progressive caseation is prone to occur while there is little attempt at healing. Most frequently the process spreads from other parts to the tube, although in some instances a simultaneous attack in several regions may occur. The secondary infection of the peritoneum from the tube is more frequent than the reverse. Primary tuberculosis in the vagina and vulva is very unusual.

Bacteriological Study of Tuberculosis of the Lymph Glands in Children.—MITCHELL (*Edinburgh Med. Jour.*, 1914, viii, 209) examined the cervical, bronchial and mesenteric lymph glands of 29 autopsies of children. Cultures were obtained in 12 cases, 8 of which gave the human type of tubercle bacillus and 4 the bovine type. Three of the latter infections also involved the meninges. The mesenteric glands were claimed to be the seat of origin of the disseminated infection. In two of the bovine infections, the cervical and bronchial glands were also diseased. Seven of the eight strains of the human type had their origin in the bronchial glands. On several occasions positive cultures were obtained from the tonsils. The cervical glands were furthermore examined in a series of 80 surgical operations. In 71 instances the

bovine bacillus and in 7 the human type was isolated. Moeller, who eight times isolated the tubercle bacillus from the sputum and lung tissue, found only the human type. In compiling the results of other authors he states that of 36 investigators 974 cases of tuberculosis of lung and bronchial glands were examined. Of these the human type was isolated 967 times, the bovine five times and both human and bovine twice.

The Relation of Tuberculosis to Various Cirrhoses.—ALLESSANDRO (*Internat. Centralbl. f. d. ges. Tuberk. Forsch.*, 1915, ix, 323) studied the changes occurring in various parenchymatous organs in relation to the connective-tissue stroma. He found that chronic tuberculosis was prone to induce a connective tissue increase in all organs, but that some were more intensely affected than others. The spleen showed the earliest and greatest fibrosis, while the liver, kidney and pancreas followed in order. The process was one whereby the normal stroma was diffusely increased accompanied by the development of an accessory reticulum throughout the tissue. These organic changes, he believes, are the direct result of toxic substances arising in a tuberculous focus. The poisons are of such character that they stimulate connective-tissue formation in each organ that is reached. The toxins are distributed by the blood stream.

Laboratory Infections with B. Typhi.—KISSKALT (*Ztschr. f. Hygiene*, 1915, lxxx, 145) has brought together various cases of typhoid fever which have been acquired during work in laboratories. These cases include not only those that have appeared in literature but also those from continental laboratories with whom he has had personal correspondence. In all, the author has collected 60 cases, many of these were the result of the accidental infection of the mouth by pipette during Widal examinations. Others were obtained during the examination of feces or urine. Of these there were 6 fatal cases. In the majority of instances of accidental infection of the mouth which had knowingly taken place, disinfection, usually with alcohol, was tried. It would appear that the stock laboratory cultures still retained high virulency for man.

Changes in the Aorta in Children and their Relation to Arteriosclerosis.—In spite of the numerous studies and animal experiments, the etiological factors of arteriosclerosis are not agreed upon. The influence of age and mechanical stress is no longer considered of as great importance as the more active agents of which infections are the most important. Experimental proof of the influence of bacteria has been brought forward by French and American investigators. Added to this, STUMPF (*Ziegler's Beitrage*, 1914, lix, 890) has studied the arteries of young children in which no evident arterial disease was recognized, but where the microscopic study demonstrated the beginning of damage in the arterial wall. The aortas of 84 children were examined. Evidence of fatty degeneration was present in 44 cases. Of these 44, 31 were suffering from chronic disease. Of 36 cases dying of acute infections, 12 showed definite arterial lesions. The chronic conditions associated with arterial degeneration were tuberculosis,

chronic suppurations and marasmus. The author believes that the influence of these chronic diseases upon the arterial wall is not directly through the toxins, but rather by the indirect action of the altered state of nutrition.

Primary Cancer of Liver in Two Sisters.—A considerable literature is available indicating the familial occurrence of cancer. To a certain extent, the occurrence of cancer in several members of a family represents chance findings particularly when the cancerous processes differ in their kind and location. It is rather striking, however, to have two individuals in the same family die of cancer of the same organ. HEDINGER (*Centralbl. f. Path.*, 1915, xxvi, p. 385) reports a primary cancer of the liver in two sisters. These came to autopsy within a week of each other. The first was aged seventy-one years, in whom the liver weighed 3900 grams. The left lobe of the liver was, for the most part, occupied by tumor masses with a small secondary in the right lung. Otherwise there were no metastases. The other sister was seventy-seven years old; the liver weighed 1980 grams and showed a white, cancerous tumor mass in the left lobe. Metastases were not present. In the second case the tumor did not seriously affect the health, but the patient died of heart disease. Cirrhosis was not present in either case.

The Development of Arteriosclerosis in the Aorta of Rabbits.—The Russian School of investigators have introduced a new method of producing experimental arterial lesions which they claim simulate the human type. These have been obtained by the feeding of cholesterin. ANITSCHKOW (*Ziegler's Beitrage*, 1914, lix, 356) criticizes the previous work in that although lesions comparable to those in man were obtained, the conditions of the experiments were very artificial. In the present work he found that by feeding pure cholesterin, positive results were obtained at the end of a month. Furthermore by increasing the blood-pressure he was able to get equal arterial changes with less cholesterin and in a shorter time. Thus moderate increase in blood-pressure and slight rise in the blood cholesterin is of great importance. The use of adrenalin and cholesterin leads to a fatty deposit in the arterial wall quite different from the commonly found adrenal necrosis. Likewise, the suspension of rabbits by the hind limbs with the exhibition of cholesterin lead to similar fatty deposits. In some instances he observed the simultaneous occurrence of hyperplasia, degeneration and cellular infiltration of the arterial wall. The author believes that the results of his experiments can be directly applied to the interpretation of the human disease.

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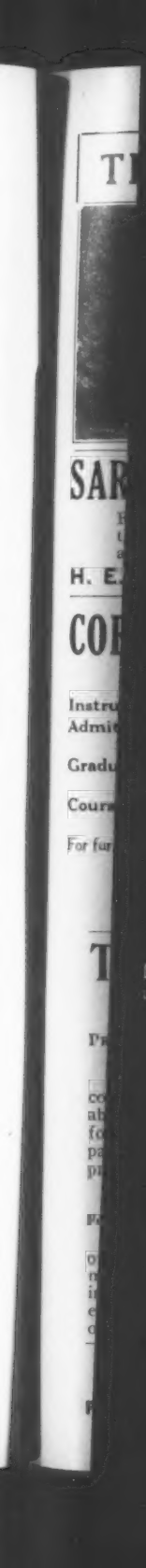

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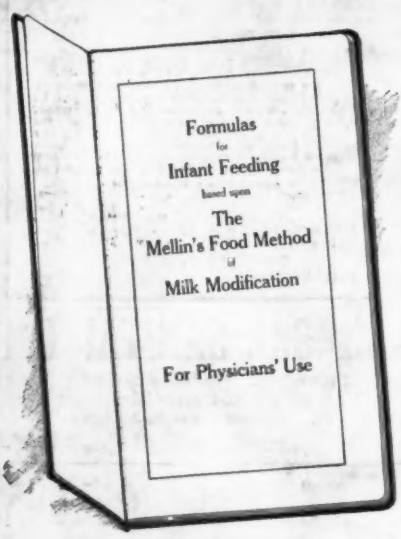

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